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DIELECTRIC CONSTANTS OF CRYSTALS

Part II. Gypsum

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(Communicated by Prof. S. Bhagavantam, F.A.SC.)

1. Introduction

It can be shown from theoretical considerations that the dielectric anisotropy of triclinic crystals is fully expressed by six independent constants, of monoclinic crystals by four, of orthorhombic by three, of trigonal, tetragonal and hexagonal by two and of cubic by one constant. In systems of symmetry higher than triclinic and monoclinic, the principal directions of the dielectric ellipsoid coincide with the principal directions of the optical ellipsoid. In the case of monoclinic system, only one of the principal directions of the dielectric ellipsoid coincides with one of the directions of the optical ellipsoid and that is also the crystallographic symmetry axis. The other two may in general make an angle with the corresponding directions of the optical ellipsoid.

2. Existing Data on Gypsum

The work on the dielectric constants of monoclinic crystals is meagre. The values[1] for crystals of sugar, Malachite, Adular and Augite obtained by different authors do not agree amongst themselves. Full data for gypsum were obtained by W. Schmidt[2] alone by a method similar to Drude's at a frequency of about 4×10^8 cycles/sec. The dielectric constant of gypsum perpendicular to the cleavage plane was determined by Curie,[3] Starke[4] and Jaeger[5] and the values vary from 5·04 to 6·3.

From Maxwell's electromagnetic theory, we get the relation $n^2 = \epsilon$. When the refractive index for the visible region is taken, this relation does not hold good except in the case of few substances like diamond. But when the anomalous dispersion of the substance is taken into account, and the refractive index for infinitely long waves obtained it comes out to be $\sqrt{\epsilon}$. Liebisch and Rubens[6] deduced the dielectric constants of many substances by observing the reflecting powers of the crystal for infra-red rays. When the refractive index for infinitely long waves, obtained from reflection data, is squared, it compared well with the dielectric constants

determined by electrical methods. Rubens[7] determined the dielectric constants of gypsum by this optical method.

There is an important discrepancy between Schmidt's and Ruben's results in the case of gypsum. The disposition of the various axes will be given before dealing with that discrepancy.

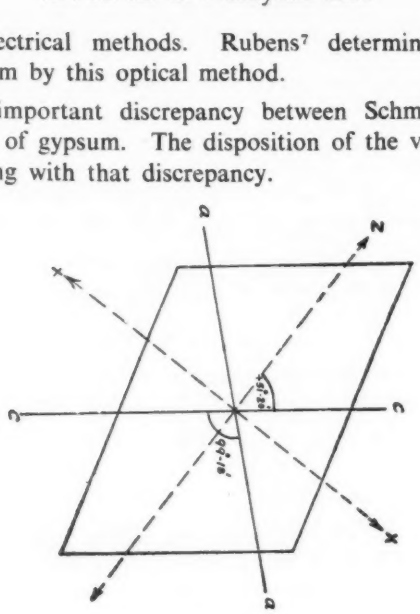

FIG. 1

Gypsum belongs to the monoclinic class with an eminent cleavage plane in (010) perpendicular to the *b*-axis. The Y-axis of the optical ellipsoid ($n_x < n_y < n_z$) lies along this axis. So the cleavage plane is the optic axial plane as well for gypsum, and contains the *a* and *c* crystallographic axes, and the X and Z axes of the optical ellipsoid. The crystallographic axis *a* makes an obtuse angle of 99° 18′ ($\angle\beta$) with *c*. The angles measured from *c* in the direction of this obtuse angle are taken positive. The Z-axis (which is the acute bisectrix) is inclined to *c* at + 52½° (at 9·4° C.) and turns through 5° 41′ towards *c* when heated to 91°. Assuming a linear variation, the inclination of the Z-axis to *c* will be + 51° 20′ at 26° C. Besides variation with temperature, there is also dispersion of the Z and X axes with wave-length.

Two of the principal axes of the dielectric ellipsoid lie in this *ac*-plane and if the principal dielectric constants in this plane are ϵ_1 and ϵ_2 ($\epsilon_1 > \epsilon_2$), the angle between the direction of ϵ_1 and *c* may be called χ and taken positive when measured in the direction of the obtuse $\angle\beta$. According to Schmidt this angle is + 102°·5 whereas Rubens gives it as − 1°·0. ϵ_1 and ϵ_2 from Schmidt's determination are 9·9 and 5·0 and according to Ruben's 11·6 and 5·4. Apart from some of these differences in the values of ϵ_1 and ϵ_2,

the discrepancy in the value of χ is important. If the relation $n^2 = \epsilon$ is valid when n for infinitely long waves is considered, then χ also should come out to be the same whether obtained by the electrical method by directly determining the dielectric constants, or by the optical method with long waves. In this connection, the orientation of the magnetic axes may be mentioned. According to Krishnan[8] the principal axes of the magnetic ellipsoid are along b, along c, and perpendicular to c in the ac-plane. So the direction of the principal magnetic axis (of larger susceptibility) is nearly coinciding (1° difference) with the direction of ϵ_1 as obtained by the optical method with long waves.

3. The Dielectric Ellipsoid

There are some differences of opinion with reference to the representation of dielectric ellipsoid. In the International Critical Tables[1] it is assumed that the value of ϵ in any direction is numerically equal to that semi-diameter of the ellipsoid $\frac{x^2}{\epsilon_1^2} + \frac{y^2}{\epsilon_b^2} + \frac{z^2}{\epsilon_2^2} = 1$, which is parallel to the given direction. This means that if an ellipsoid is drawn with its principal semi-diameters equal to ϵ_1, ϵ_b, ϵ_2, its radius vector in any direction will give the dielectric constant in that direction. From the above equation, it can be seen that if l, m, n are the direction cosines, ϵ_{lmn} will be given by

$$\frac{1}{\epsilon^2_{lmn}} = \frac{l^2}{\epsilon_1^2} + \frac{m^2}{\epsilon_b^2} + \frac{n^2}{\epsilon_2^2}. \qquad \text{(I)}$$

On the other hand, if we assume Maxwell's relation $n^2 = \epsilon$ to hold good, the dielectric anisotropy may be represented by either the Fletcher indicatrix or the Fresnel ellipsoid. For getting the Fletcher indicatrix, the ellipsoid is to be constructed with its principal semi-diameters equal to $\sqrt{\epsilon_1}$, $\sqrt{\epsilon_b}$, $\sqrt{\epsilon_2}$ and for getting the Fresnel's ellipsoid the semi-diameters should be $\frac{1}{\sqrt{\epsilon_1}}, \frac{1}{\sqrt{\epsilon_b}}, \frac{1}{\sqrt{\epsilon_2}}$. The equation of the Fresnel ellipsoid will be

$$x^2\epsilon_1 + y^2\epsilon_b + z^2\epsilon_2 = 1$$

$$\text{or} \quad l^2\epsilon_1 + m^2\epsilon_b + n^2\epsilon_2 = \epsilon_{lmn}. \qquad \text{(II)}$$

The experimentally determined dielectric constant in any direction should agree with that given by (II) and not by (I). This investigation shows it to be so, besides clearing up the discrepancy in the value of χ.

4. Experimental Results

The principal optical directions (Z and X) contained in the cleavage plane are marked on a perfectly transparent lump of gypsum by an examination of a thin section of it under the polarising microscope. The crystallo-

graphic *c*-axis is recognised by cleavage lines developed in the thin section. Whether that direction is along *c* are not is verified by a magnetic experiment. When the section is suspended in a uniform magnetic field with a silk fibre, the plate oriented itself such that the cleavage lines mentioned above are parallel to the magnetic field, showing that it is the direction *c*. On the crystal lump Z, X and *c* are marked out. Four sections, cut from the lump for the present investigation, have their normals making the angles − 46° (I), − 4° (II), + 44° (III) and + 86° (IV) with the Z-axis or + 5° 20′, + 47° 20′, + 95° 20′ and + 137° 20′ respectively with the *c*-axis.

The above four plates and another one perpendicular to the *b*-axis are used in the present investigation and the dielectric constants perpendicular to their planes are determined. The method employed is the same as that described in an earlier communication by the author.[9]

In determining the dielectric constants of the neutralising liquid mixture which has the same constant as the crystal section in question, the value of benzene was taken to be 2·27 at the room temperature 26° C., for finding the leads correction to the liquid cell. The values were determined at a frequency of 1·6 mega cycles per second.

10·6 (ϵ_I), 7·95 (ϵ_{II}), 5·3 (ϵ_{III}), 7·7 (ϵ_{IV}) are the values obtained with the four sections respectively. As the normals to the sections make the angles + 5° 20′, + 47° 20′, + 95° 20′ and + 137° 20′ with the *c*-axis, the above are respectively the dielectric constants at those inclinations. 5·25 is the value found perpendicular to the cleavage plane.

The principal dielectric constants ϵ_1, ϵ_2, ϵ_b and the angle χ calculated from the above data are given in Table I, together with the values of previous authors.

TABLE I

Frequency	ϵ_1	ϵ_2	ϵ_b	χ	Investigator
$1{\cdot}6 \times 10^6$	10·60 (10·61)	5·30 (5·27)	5·25	+ 2° (+ 2° 6′)	Author
4×10^8	9·92	5·04	5·15	+ 102°·5	Schmidt
1×10^{12} (Optical)	11·6	5·4		− 1°	Rubens
1×10^{12}			7·5		Rubens[10]
Audio			6·3		Curie
10^5 to 10^7			5·1		Jaeger
Audio			5·04		Starke

5. Discussion of Results

For calculating ϵ_1, ϵ_2 and χ either equation I or equation II given in Section 3 is to be used. Directions I and III are mutually perpendicular

to each other and so are II and IV. All the four are in the cleavage plane. So the direction-cosine (m) with respect to b-axis is zero. The dielectric constant ϵ_1 in the cleavage plane should be given by

$$\frac{1}{\epsilon_1^2} = \frac{l}{\epsilon_1^2} + \frac{n^2}{\epsilon_2^2}$$

according to equation I, where l and n are the direction-cosines. When we take the direction III which is perpendicular to I, we get

$$\frac{1}{\epsilon_{III}^2} = \frac{n^2}{\epsilon_1^2} + \frac{l^2}{\epsilon_2^2}$$

and therefore

$$\frac{1}{\epsilon_1^2} + \frac{1}{\epsilon_{III}^2} = \frac{1}{\epsilon_1^2} + \frac{1}{\epsilon_2^2}.$$

This relation should hold good for any two mutually perpendicular directions in a principal section and we have

$$\frac{1}{\epsilon_{II}^2} + \frac{1}{\epsilon_{IV}^2} = \frac{1}{\epsilon_1^2} + \frac{1}{\epsilon_2^2}$$

or

$$\frac{1}{\epsilon_1^2} + \frac{1}{\epsilon_{III}^2} = \frac{1}{\epsilon_{II}^2} + \frac{1}{\epsilon_{IV}^2}.$$

When the same reasoning is applied to equation II, we get

$$\epsilon_I + \epsilon_{III} = \epsilon_{II} + \epsilon_{IV}.$$

From Table II, the applicability of equation I or II will be evident.

TABLE II

$\frac{1}{\epsilon_I^2} + \frac{1}{\epsilon_{III}^2}$	$\frac{1}{\epsilon_{II}^2} + \frac{1}{\epsilon_{IV}^2}$	Difference	$\epsilon_I + \epsilon_{III}$	$\epsilon_{II} + \epsilon_{IV}$	Difference
·0445	·0327	30·6%	15·9	15·65	1·6%

The values calculated from equation II are thus in agreement within experimental errors. The values calculated from equation I do not agree at all with each other. It is evident from the experimental results that the reciprocal of $\sqrt{\epsilon}$ in any direction is given by the radius-vector in that direction, if the principal axes of the ellipsoid represent the reciprocals of the square roots of the principal dielectric constants. When the ellipsoid is constructed with the principal axes representing the principal dielectric constants themselves, the radius vector in any direction is not giving the dielectric constant in that direction. The above findings are in consonance

with the applicability of Maxwell's relation $n^2 = \epsilon$ for crystals of all classes, with the proviso that n is the refractive index for infinitely long wave-lengths.

Using the equation II, ϵ_1, ϵ_2 and χ are calculated from the experimental results and given in Table I. It is seen that χ obtained from electrical data in the present investigation is very near that obtained by Rubens by the optical method. It should be expected so if the relation $n^2 = \epsilon$ is to be applicable to any class of crystals, when n for infinitely long waves is taken. These directions are inclined to X and Z of the visible region and this may be due to the dispersion of the axes with wave-length in monoclinic and triclinic classes.

It is interesting to note that the magnetic principal direction (of higher susceptibility) is almost coincident with that of the electrical susceptibility. Small differences obtained in the angles may be due to slight experimental errors. It is possible that the principal directions of the dielectric ellipsoid obtained by the electrical method or the optical method, and the principal directions of the magnetic ellipsoid are the same, though different from the crystallographic axes in the case of monoclinic or triclinic crystals. It is proposed to carry on investigations on these lines, with a few other monoclinic crystals.

6. Summary

The dielectric constants of gypsum in a number of directions are determined by a modified liquid mixture method and the values are found to fit into the formula $\epsilon_{lmn} = \epsilon_1 l^2 + \epsilon_b m^2 + \epsilon_2 n^2$ where ϵ_1, ϵ_b, ϵ_2 are the principal values, and ϵ_{lmn} is the constant in any direction with direction-cosines l, m, n. The values do not fit into the alternative relation,

$$\frac{1}{\epsilon^2} = \frac{l^2}{\epsilon_1^2} + \frac{m^2}{\epsilon_b^2} + \frac{n^2}{\epsilon_2^2}.$$

There was a discrepancy in the value of χ (angle between the direction of ϵ_1 and the crystallographic c-axis) as obtained by Schmidt by an electrical method, and as obtained by Rubens by an optical method on the basis of Maxwell's relation $\epsilon = n^2$ applicable for n for infinitely long waves. χ in the present investigation has come out nearly to be the same as that obtained by Rubens and so lends support to the applicability of $\epsilon = n^2$ in this case also. It is further found that the principal directions of the dielectric ellipsoid are almost coincident with the principal directions of the magnetic ellipsoid.

The author wishes to record his grateful thanks to Prof. S. Bhagavantam or his helpful guidance during the progress of this work.

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THE INFLUENCE OF SUBSTITUENTS ON THE ADDITIVE REACTIVITY OF ETHYLENE DERIVATIVES

Part V. Further Consideration of the Mechanism of Bromine Addition

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Received January 9, 1948

In Part IV of this series,[3] a tentative mechanism was suggested and subsequent work[1, 4] led to some modification of the scheme without affecting the essential features. Investigations in the gas phase and in solution in different laboratories clearly revealed the complex nature of the reaction,[5, 6, 9] the salient features being the following:

(i) The reaction is of the first order with respect to the olefine;

(ii) At temperatures below 27° C. the reaction appears to be a termolecular one involving the square of the bromine concentration;

(iii) Activation of the double bond can be either internal or external. In some cases, both activations may be present;

(iv) Catalytic activation is of primary importance if internal activation is inadequate or if deactivating groups are present;

(v) The thermal reaction involves only the polarised halogen molecule and the ethylene derivative, the rate-determining step not involving full charge separation.

Further, the influence of substituents may not be the same in the gas phase and in solution and may vary also with the solvents.

In the comparison of reactivity using only the velocity constants, either directly determined or evaluated by a competitive method, there is the implicit assumption that the frequency factor is identical for all the olefines examined. This assumption is by no means justified as one finds from a careful analysis of the experimental facts.

Changes in the solvent as also variation of substituents appear to require, as will be observed in later sections of this note, a change in the mechanism of addition, and this behaviour also indicates velocity constant as quite an inadequate criterion for evaluating group influences. Only

crotonic acid (trans) appears to be common to more than one solvent and serves to link observations at different temperatures and different solvents. A fuller picture of the position is possible by taking into consideration not only the velocity constant but also the other parameters of the rate constant equation.

In an earlier publication,[4] it was noticed that the reaction can be classified as a 'slow' one with frequency factors several powers of ten lower than what might be expected for a bimolecular reaction and the suggestion was made there that the encounter frequency calculated by the usual collision formula should be corrected for orientation effect by a term which can be approximately taken as a function of the bond-distance of the bond involved in the reaction and the molecular dimension of the reactants evaluated from known values of bond distances and bond angles. The effect of such a correction can be seen in a few cases in Table I.

TABLE I

Compound	k_2 at 35°·5 C.	E (kilocalories)	PZ (Obs.) at 35°·5	PZ (calc.) using corr. term.
trans-Crotonic acid ..	0·0379	10·8	$1·95 \times 10^6$	$8·9 \times 10^6$
Tig'ic acid ..	0·1995	6·8	$1·36 \times 10^4$	$0·95 \times 10^6$
$\beta\beta$-Dimethyl acrylic acid	0·773	7·2	$4·43 \times 10^4$	$0·95 \times 10^6$

The agreement between the last two columns indicates that smallness of the frequency factors is largely due to the need for an encounter in the region of the bond affected. Since a solvent may not be expected to appreciably influence such encounters in the case of reactions between essentially neutral molecules or between the polar molecules and the non-polar molecule, solvent influence must be primarily on the energy of activation while substituents alter both factors.

In the light of these observations we can now consider the results of the competitive methods. The standard for comparison has been naturally the unsubstituted ethylene and the reaction studied is the one catalysed by hydrogen bromide. If the Arrhenius parameters for this compound can be evaluated, the competition results enable the evaluation in other cases. The reaction has been studied by the author only at 18° C.[2] and the frequency factor and energy of activation can be evaluated only by calculating the 'collision' number with the correction term using the data for the catalysed reaction. Even the unsubstituted ethylene has been found to show pronounced autocatalysis and an induction period in non-hydroxylic solvents,

which can be eliminated only by using a catalyst. It is found that the reaction can be represented by the equation:

$$\ln k = 22{\cdot}9028 - \frac{13{,}750}{RT}$$ (k in moles/litre sec.$^{-1}$; R in calories/mole.)

It is not without significance that the value of the energy of activation obtained here is considerably below the value calculated by Eyring's method.[9] This will be considered in a later section. Using the value obtained for ethylene, one can proceed to evaluate the parameters for the other compounds. In the competitive method, since equivalent concentrations had been used, the error will not be very large if one considers that the frequency of encounter between the ethylene derivative and bromine is not very different for the olefines compared. With this assumption we have the relation

$$\frac{k_x}{k_y} = \frac{P_x e^{-E_x/RT}}{P_y e^{-E_y/RT}}$$

Using this the Arrhenius parameters in a number of cases can be evaluated and the results are tabulated in Table II.

TABLE II

All the values refer to reactions in methylene chloride solution. Though competition experiments had been carried out only at -35° and -78°, it is assumed that the reduced velocity remains the same at the higher temperature also. T: 18° C. Concentrations: 0·1 M.

Compound	k moles/litre sec.$^{-1}$	P	E. K. Cal. from Eqn. 1	E. K. Cal. from ν^2/E curve	Raman frequency ν cm.$^{-1}$
Ethylene ..	0·26	0·042	13·75	13·75	1623
Protylene ..	0·53	0·034	13·40	13·36	1647
Isobutylene ..	1·43	0·033	13·00	13·30	1650
Trimethyl ethylene ..	2·70	0·022	12·60	12·85	1679
Tetramethyl ethylene ..	3·64	0·022	12·50		(1685)
Vinyl Chloride ..	0·008	0·037	15·05	(14·10)	1608
Acrolein ..	0·390	0·033	13·50		(1626)
Crotonaldehyde ..	0·78	0·022	13·20		(1640)
Acrylic acid ..	(0·039)	(0·033)	(14·20)		(1600)
Crotonic acid ..	0·068	0·020	14·25		(1598)
Styrene ..	0·83	0·028	13·15		1631

Note.—All the values for acrylic acid are extrapolated values. Values in brackets in the last two columns are obtained from $\nu^2 - E$ curve.

It will be observed that for considerable variations in the rate constant, the changes in the activation energy are not large. Since the reaction involves a change in the carbon-carbon bond distance from that of a double bond to that of a single bond, some correlation may be expected between the activation energy and the force constant of the double bond or, what

leads to the same result, to the square of the Raman frequency. The existence of a correlation can be observed from the ν^2—E curve (Fig. 1).

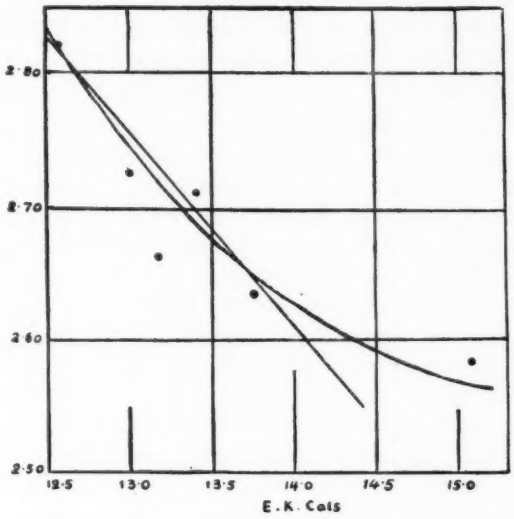


FIG. 1

The figures in the fifth column of Table II give the values of the activation energy assuming the linear relationship while the last column gives also the Raman frequency values corresponding to activation energies in Column 4 for the remaining substances. The possibility of deviations where deactivating groups are present cannot be overlooked when one sees the wide discrepancy between the E values of vinyl chloride and further in this note, this aspect is also considered.

It was mentioned earlier that crotonic acid serves as a link in considering solvent influences. The value obtained for the activation energy in methylene chloride is found to be over 3 K. cals. higher than in acetic acid and the same might be expected also in other cases. At least a part of this energy of activation must be the energy required for stretching the carbon-carbon bond a distance of about 0·2 Å, *i.e.*, the value of about 7·2 K. calories. For the dissociation of bromine into two normal atoms, an energy of about 46·1 K. cals. is needed but, from all present observations, the addition reaction involves only the polarised molecule and not either atoms or ions of the halogens and this should involve much smaller values, altered further by the dielectric constant of the solvent. One may picture the activation energy as a composite function involving the following:

(i) The polarisation of the double bond (*a*) by internal factors, and (*b*) by external catalysts;
(ii) The polarisation of the bromine molecule;
(iii) The resonance energy of the rate determining step in the reaction. This will be influenced by substituent groups.

With unsubstituted ethylene and carbon tetrachloride as solvent, conditions approximating to a gas reaction but the possibility of heterogeneity stands in the way of using it as a suitable solvent. However, it is worth while taking the results obtained in this solvent also.[11] Proceeding as in the case of the methylene chloride solution and with a reaction catalysed by hydrogen bromide (1 mole of catalyst to 4 moles of bromine) the meagre data available leads to a value for the energy of activation for ethylene-bromine reaction of about 11 K. cals. Lower catalyst concentrations can be expected to slow down the rate and one can safely conclude that the activation energy of the reaction in methylene chloride is not very different from that of carbon tetrachloride even though it provides a more polar environment for the reactants. It is, however, possible that with substituted olefines having a definite dipole moment, the polarising influence of this solvent may serve to reduce the activation energy. This influence should be even more pronounced in the case of the hydroxylic solvent, acetic acid as is found to be the case. The influence of substituents is a more complex picture.

The olefinic acids studied showed that as temperatures are raised and with an increase in the number of activating groups, the influence of the catalyst on the reaction diminishes. Obviously comparisons of reactivity can have any meaning only if identical conditions are present. This may be presumed to be the case if we take crotonic acid and compounds with either deactivating groups or with insufficient activating groups. It has been pointed out in the earlier parts that if a solvent functions as a catalyst, it does not alter the relative velocities so that k_y/k_x should be a constant not only at different temperatures but also in different solvents. Taking crotonic acid and ethylene as our test cases, the following results are obtained:

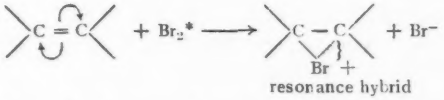
Temperature: 49·95° C.
Concentration: M/30
k_y/k_x : 0·26 (k_y: velocity constant of crotonic acid)
k_y : $8 \cdot 52 \times 10^{-2}$ moles/litre sec.$^{-1}$

Solvent	E_x	E_y	E_x/E_y
Methylene chloride ..	13,750	14,250	0·965
Acetic acid ..	10,600*	10,860	0.976

* Value calculated from k_y, reduced velocity and corrected frequency factor.

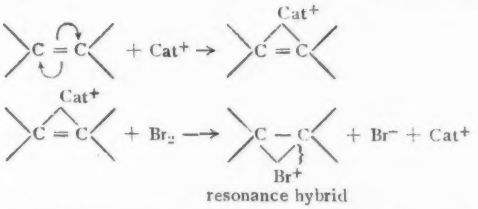
The agreement in the last column justifies the basis of comparison adopted and enables an analysis of the results of mutual group interactions in affecting the reactivity of the double bond. With substituents of Class 1[6], the result of activation is to lower the activation energy which is essentially a linear function of the force constant of the bond. Consequently, asymmetry has a pronounced effect. The introduction of deactivating groups on the other hand leads to deviations which possibly involves a mechanistic change. The greater the deactivation, the more pronounced the influence of the catalyst of which higher relative concentrations are needed. This condition can be altered by an electron sink which can facilitate initiation of attack by the negative part of the polarised bromine molecule, the influence of hydrogen bromide as a catalyst becoming a negligible factor. The gradation can be pictured as follows, taking into account only the rate determining step of the reaction for giving a ' bimolecular ' constant:

Group I.—Uncatalysed: Polarisation of double bond by substituent groups. Two or more substituents of Class 1 + I; Substituents of Class 5 + I + T



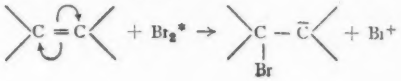
Inter-conversion of cis-trans isomers possible during addition.

Group II.—Reaction catalysed by hydrogen ions, halogens as cations and possibly other cations: Unsubstituted ethylene. One substituent of Class 1; Substituents of Class 4, 6, 7: −I + T, + I − T, ± T; Carboxylic acids.



Inter-conversion of cis-trans isomers will be a normal feature.

Group III.—Uncatalysed reaction. Polarisation of double bond by substituent groups facilitating initiation of attack by negative part of the polarised bromine molecule: Class 5 − I − T other than carboxylic acid. It is possible that some members of Class 7 (− T) and members of Class 2, − I, also come under this category.



Inter-conversion of cis-trans isomers may not take place.

While the grouping given here can be expected to hold good with mono-substitution products and with polysubstitution products of Class 1 generalisations are more difficult when several substituents belonging to different classes are present. An increase in the number of Class 1 substituents can more than compensate for the presence a single deactivating group of classes in Group II so that the reaction takes place by the mechanism of Group I. In a similar manner, loading with three or four substituents of the carboxyl type or of Class 7 $\pm$ T, can make the mechanism of Group III possible but the large size of the Br^- and the steric effects of the substituents result in the absence of the addition compound.

In comparing the influence of substituents on reactivity, conditions can be expected to be the same only for members in the same group within which quantitative comparisons will be accurate but deviations invariably can be noticed when there is a mechanistic change. This is well brought out when one compares the relative influence of methyl groups as expected from the competition studies with the influence in the case of alkyl acrylic acids. Mention should also be made here of the possibility of a change from mechanism of Group II to that of Group I even in the same substance with changes in temperature so that activation energies appear to give abnormal values.

It may be remarked that in the postulated mechanisms, there is no indication of the termolecular reaction observed by Robertson and co-workers[6] as well as the gas reaction studied by Gwyn Williams.[5] These observations are, however, quite consistent with Group II, one molecule of bromine serving as the 'catalyst'. One can also visualise the reacting bromine molecule as the polymer Br_4 which reacts in the polarised form $\overset{\delta+}{Br} - \overset{\delta-}{Br_3}$. At higher temperatures, especially in polar solvents, conditions for such a reactant are not likely, dissociation into Br_2 molecules taking place, with hydrogen-ion and similar catalysts taking control. The change in slope of the log k/1/T curve reported by the author[4] is a pointer in this direction.

It is necessary also to deal with possible complications due to the peroxide effect noticed by Kharasch and co-workers[7] with other reactions of olefines. In the absence of positive evidence of peroxide formation, this does not invalidate any of the conclusions regarding substances conforming to the mechanism of Group I. In Group II, it has been shown that carboxylic acids are not affected. In the case of others, the negative catalysis by this complication can be expected to make the activation energy higher than should be the case if deactivating substituents are present. This may

account for the difference between calculated and observed values of activation energy in the case of vinyl chloride. It is quite possible that vagarious results obtained by Venkatraman[10] with crotonaldehyde are due to variations in the peroxide content, the formation of which may be expected to favour mechanism III by providing an additional electron sink.

Summary

The influence of substituents on the additive reactivity is reconsidered with particular reference to the Arrhenius parameters. Using the correction terms for the frequency factor in order to account for correct orientation of reactants, the activation energy of ethylene and a number of ethylene derivatives have been calculated. The correlation with the bond stretching force constant and the grouping together of ethylene derivatives on the basis of mechanistic differences follows from these results. The mutual action of groups and the peroxide effect are briefly considered. The solvent affects essentially the activation energy of the rate determining step.

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CONCENTRATION OF GRAPHITES FROM THE EASTERN GHATS

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Introduction

Graphite occurs as a frequent accessory mineral disseminated in the Khondalites of the districts of Kistna, Godavari and Vizagapatam in the Madras Presidency. Pegmatite and Quartz veins cutting through the graphite-bearing khondalites occasionally contain lenses and pockets of graphite. It is sometimes observed that these lenses extend from the intrusives to the country rocks also, namely, khondalites. Frequently bands of crystalline limestone run for long distances parallel to the graphite-bearing pegmatites and quartz veins but this is by no means a universal feature. Sometimes the normal khondalites and occasionally even the quartzitic bands in the khondalites contain graphite.

The better grades of graphite mined from a few localities in West Godavari District and in the contiguous parts of the Nizam's Dominions are brought to Rajahmundry and exported in a raw state. Some of the less pure varieties are used after crude washing for the manufacture of crucibles at Rajahmundry by admittedly primitive methods. A good part of the graphite which assays less than 55% carbon is at present being discarded. This is a colossal and preventable loss. The increased uses of graphite demand the purification of these low grade graphites.

There are two types of impurities met with in graphite. One is the inherent ash which is present probably in intimate association with the carbon. It is almost impossible to dislodge this impurity by any simple device. But the more frequent impurity, which brings down the assay value of the sample, is the extraneous mineral matter in fine grains which can be removed by physico-chemical methods such as froth flotation.

In American practice various methods are used for concentration and refining of low grade ores.[1] The Bureau of Mines, U.S.A.[2] has worked out flotation processes for the concentration of very low grade oxidised and unoxidised graphite ores from Alabama, New York, assaying 5–10% graphitic carbon. Acid ranges were recommended for the froth flotation.

Enrichment to 90% carbon with 70–80% recovery has been shown to be possible.

Pine oil was found to be one of the most satisfactory frothing and collecting agents, especially in the acid pulps for both oxidized and unoxidized ores.

J. C. Ghosh, K. Banerjee and M. R. Aswathanarayana Rao[3] investigated the possibilities of the concentration of Indian graphites by froth flotation. They have tried a number of frothers, collectors and depressants and also carried out flotations at different pH values of pulp. The samples used were mostly about 60% carbon content and a few of 30% carbon ground to 90–200 mesh. They concluded that the Indian graphites can be benificiated to a fair degree of purity by froth flotation methods. They have not however mentioned the optimum pH and the particle size. Further, according to them the hydraulic classification was ineffective for separation, due to the close proximity of densities of Gangue (quartz) and graphite.

The velocity of a particle experiencing eddying resistance is proportional to square root of D as represented in the equation below:

$$U = K_e \sqrt{\frac{D(\rho^1 - \rho)}{\rho}}$$

when U = Linear velocity of the particle.
D = diameter " "
ρ^1 = density of the substance.
ρ = density of classifying liquid.
K_e = constant.

From the above equation it follows that even if the densities are very close, if we can bring about differentiation in grain size between graphite and quartz, hydraulic classification should be possible. Since the hardness of graphite is about 1 on Moh's scale when compared with that of the Gangue containing mostly quartz and felspar 6 to 7 on Moh's Scale, selective grinding can be readily accomplished.

The object of the present work is to examine and ascertain the commercial possibilities of concentrating crude graphite of low grades containing about 50% carbon from Godavari and Vizagapatam areas. Investigations were along the following main lines:

(i) Selective grinding and hydraulic classification.

(ii) Froth flotation, effect of grain size and pH variation.

(i) Selective Grinding and Hydraulic Classification

A small rod mill containing cylindrical iron rods with tight rubber sheaths is used to grind the material wet (50% solids). After a few preliminary experiments the optimum speed and load for the mill are fixed. The product obtained after grinding for long period was sieve analysed.

The product sieve analysis:

Mesh	Quantity	% Carbon
−5–10	4·0 gr.	43·1
−10–16	7·5 „	45·8
−16–36	5·0 „	46·0
−36–50	4·0 „	48·7
−50–80	2·0 „	49·3
−80–100	3·5 „	54·2
−100–200	3·1 „	59·6
−200	10·0 „	68·1

The material passing through 200 mesh and which analysed 68·1% was elutriated in an Andrews Elutriator. The material thus classified was separately weighed and analysed. The results are given below:

Mesh	Weight	% Carbon
250-mesh	4·5 gr.	50·1
800 „	2·3 „	79·8
above 800 „	3·2 „	85·0

(ii) Frota Flotation

A sample of graphite (C−33%) from Kurupam was subjected to differential grinding as before and the product sieve analysed. Various fractions were then froth-floated in a small cell of the type of Callow's using pine oil as frother and collector.

Table

Experiment No.	Mesh	Fraction C%	Froth C%	Gangue C%	Recovery
1	50	20·8	36·4	14·7	49·0
2	60	23·4	40·8	16·5	49·4
3	80	27·8	36·3	23·7	42·4
4	100	36·4	51·6	29·8	42·5
5	150	40·0	58·4	32·3	43·2

Froth flotation of a sample (C%—34·1) ground to pass through 60 mesh as 10% slurry with 0·2 c.c. pine oil per litre, along with the conditioning reagents was carried out and the results given in the following table.

TABLE

Experiment No.	Flotation mixture	pH	Froth C%	Gangue %	Recovery
1	No conditioning ..	8·5	50·8	17·0	74·5
2	Sulphuric acid ..	5·5	48·2	18·5	74·2
3	do do ..	5·0	48·2	18·6	74·0
4	Acetic acid ..	6·0	51·5	16·8	75·2
5	Oleic acid ..	8·0	54·5	16·9	73·0
6	Sodium silicate ..	8·5	54·7	16·2	74·6

In experiments 2, 3 and 4, the pH was varied between 5 and 8 by conditioning the pulp with the addition of acid. The pH of the sample without any acid was 8·5. There was no improvement in recovery on reducing the pH. In experiment No. 5 oleic acid was used as the collector. This results in considerable improvement with regard to recovery in addition to the fact that the froth was fragile and the suspension of graphite settled freely facilitating easy separation. The addition of sodium silicate as a depressant increased the pH value to 9 and gave good results, but in the separation of suspended solids from the froth or Gangue suspensions, much difficulty was experienced.

CONCLUSION

From the above results it is clear that the purification of graphite of low grade can be effected by a series of mechanical operations which are simple in nature. Selective grinding of the material and hydraulic classification of the same may be used as a step preliminary to the froth flotation to increase the capacity of the plants. It is concluded that with pine oil as frother, oleic acid as the collector, the froth flotation gives best results.

The authors wish to express their thanks to Prof. C. Mahadevan and Dr. K. Neelakantam for their keen interest in the work.

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CONDENSATION OF ALDEHYDES WITH AMIDES

Part XIV. Condensation of *n*-Heptaldehyde

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In the papers so far published in this series, the condensation and the conditions of condensation of eighteen aldehydes with more or less common amides have been studied. Almost all the aldehydes have been aromatic: cinnamaldehyde and dihydrocinnamaldehyde being the only exceptions, in the sense that, though each contains a benzene ring, the aldehyde group is not situated on the ring but is on the side chain.

A straightforward study of the condensations of aliphatic aldehydes with amides has not so far been undertaken. Literature abounds in the condensations with amides of the three common aliphatic aldehydes, *viz.*, formaldehyde, acetaldehyde and chloral. In the present paper are included some condensation-studies of *n*-heptaldehyde (œnanthaldehyde), a straight-chain aliphatic aldehyde, resembling benzaldehyde in so far as both contain C_7.

Medicus (1871)[1] has reported *n*-heptylidene-*bis*benzamide and *-bis*-nitrobenzamide by following the method of Roth[2] and Schuster.[3] *n*-Heptaldehyde has also been reported to have been condensed with urea by Schiff[4] to give œnanthylidene-diurea and diœnanthylideneurea, and also with thiourea (Schiff[5]). The yields have not been given.

It has been found in this laboratory that *n*-heptaldehyde condenses with acetamide, propionamide, urea, benzamide and cinnamamide, under varying conditions, giving different yields of the *-bis*amide type of product, and that it does not combine, under the same conditions, with formamide, *n*-butyramide and *n*-heptamide. Its failure to condense with formamide is not a surprise, because, of the 18 aldehydes so far examined, several have already failed to do this, but the other two amides had so far reacted very well.

As indicated by their properties and by analysis, the products of the condensation, wherever condensation did occur, were the heptylidene-*bis*-amides, the yields being generally below 50%, except in the case of propionamide which gave a 78% yield as the highest. Cinnamamide also reacted well, and gave slightly less than a 50% yield in a much shorter time (4 hours).

The conditions of the maximum yield were not identical in every case (*vide* Table). A comparison with the benzaldehyde-amide condensation (Bhatnagar and Pandya[6]) is also instructive, showing the differences in the yields when the condensation of the amide took place with an aromatic aldehyde and with an aliphatic aldehyde with the same number of carbon atoms (Table). It is noted that a pyridine-trace improves the yield, though in some cases only.

TABLE

Amides	From Benzaldehyde[6] maximum yield %	M.P.	Conditions	From *n*-heptaldehyde yield %	M.P.	Conditions
Formamide ..	18	246°	Heated, small flame, 2 hrs alone	0	..	Under all conditions tried
Acetamide ..	55	245°	Alone, water-bath, 18 hrs.	43·9	176°	Alone, 14 hrs., at 120°–150°
Propionamide ..	30·7	220°	Alone, 8 hrs. 100–20°	78·1	150°	With pyridine and piperidine, both in traces, 100–12, 5 hrs.
n-Butyramide ..	86	170°	Alone, 8 hrs., 100–30°	..	..	..
n-Heptamide ..	48·2	124°	Alone, 9 hr. 100–30°	..	..	..
Benzamide ..	23	217·5°	Pyridine trace, 6 hrs, water-bath	35·9	128°	Alone, water-bath 10 hrs.
Cinnamamide ..	80	216°	130° 4 hrs., + 160° 5 hrs., alone	46·8	200°	Alone, 120–25°, 4 hrs.
Urea ..	Not tried	..	..	34·7	160°	Alone, 110–15° 15 hrs.

(Only maximum yields are given.)

Some of these condensations were first investigated here by Norman Phœnix David after he had studied the œnanthaldehyde-malonic acid condensation (M.Sc. Thesis, 1946, unpublished).

EXPERIMENTAL

Condensation with Acetamide without any Condensing Agent

1. *n*-Heptaldehyde (1 g.) and acetamide (2 g.) (1 : 4 mol.) were heated in a 50 c.c. round-bottomed flask, fitted with an air-condenser, on water-bath, for six hours, when a homogeneous yellow solution remained. Copious steam vapours had come out. The next morning a cold yellow paste was observed; a test-portion on treatment with ether completely dissolved, showing that little or no reaction had taken place. The flask was again heated (water-bath) for eight more hours, when a yellow solid was formed. It was washed with cold distilled water, crushed in a mortar, first with cold

water and then with ether; a white product remained, which was recrystallised (cold absolute alcohol) into milk-white crystals. It did not decolorise bromine or Baeyer's reagent, suggesting absence of unsaturation. It also gave no colour with cold sulphuric acid. It melted at 166° C. and smelt very much like œnanthal, even after several recrystallisations. The yield was 0·63 g. or, as *bis*-acetamide, 33·7% of theory.

N, found: 13·39%; *n*-heptylidene-*bis*acetamide $C_{11}H_{11}N_2O_2$ requires 13·08%; *n*-heptylidene-*mono*-acetamide $C_9H_{17}NO$ requires 9·52%.

2. *Condensation at* 120–50°.—The above experiment was repeated at the higher temperature (18 hours). The contents assumed a red colour. The product melted, after recrystallisation, at 166°. The yield was 0·82 g., or 43·9% of theory.

3. *Condensation on Water-bath in* 1 : 2 *mol. proportion.*—The total heating was for 18 hours, the product was identical, but the yield was only 0·19 g., or about 10·2% of theory.

4. *Condensation in the Presence of a Trace of Pyridine.*—*n*-Heptaldehyde (1 g.), acetamide (2 g.) and pyridine (2 drops) were heated (1 : 4 : 0·15 mol.) on water-bath, without a condenser for 18 hours. The yellowish-red solid on usual treatment gave the same product, yield = 0·6 g., or 32·1% of theory.

5. *Condensation in the Presence of Pyridine-acetate.*—The same amounts of the aldehyde and the amide were mixed with 2 drops of pyridine and 2 drops of glacial acetic acid, and the whole was heated on water-bath for 15 hours: when 0·34 g. of the same product was obtained (yield 18·2% of theory).

6. *In the Presence of Glacial Acetic Acid.*—*n*-Heptaldehyde (1 g.), acetamide (2 g.) and glacial acetic acid (2 g.) (1 : 4 : 4 mols.) were heated on an oil-bath at 120-25° for 15 hours; the same product came out, yield 0·4 g. (21·4% of theory).

Condensation with Propionamide without any condensing Agent.

1. *n*-Heptaldehyde (0·5 g.) and propionamide (0·75 g.) were heated together on water-bath for 5 hours (air-condenser). The product, after recrystallisations (absolute alcohol), came out in white needle crystals, melting sharply at 150°. Like the *bis*-acetamide, it was soluble in benzene, chloroform and acetone, and all other properties of the two were similar. N, found: 11·64%; *n*-heptylidine-*bis*propionamide $C_{13}H_{26}N_2O_2$ requires 11·57%; the *mono*-amide $C_{10}H_{19}NO$ requires 8·28%. The yield was 0·8 g., or 76·2% of theory.

2. *Condensation in the Presence of a Trace of Pyridine.*—*n*-Heptaldehyde (0·5 g.), propionamide (0·75 g.) and pyridine (2 drops) (1 : 2 : 0·15 mol.) were heated on water-bath (5 hours). The reaction was more quick and the product was identical with the earlier one. Yield 0·75 g. (71·4% of theory).

3. *Condensation in the Presence of a Pyridine-piperidine Mixture.*—To the same amounts of the aldehyde and the amide, one drop of pyridine and one drop of piperidine were added. The heating was on water-bath (3 hours) and on oil-bath (112°, 2 hours). The crude yellowish product was identical; yield 0·82 g. (78·1% of theory).

4. *Condensation in the Presence of a Trace of Pyridine at higher Temperature.*—The same experiment (No. 3) was repeated with pyridine alone at 112°, but did not prove satisfactory. 10 hours' heating gave some resin. The yield was less, 0·69 g. (64·8% of theory).

Condensation with Formamide

This did not take place, when (1) the aldehyde and the amide (one gram each) were heated alone on water-bath (16 hours) in the absence of any condensing agent, (2) they were heated on an oil bath (140–45° C.) for 4 hours, (3) they were heated for 4 hours in an alcoholic medium, (4) they were heated for 4 hours with sodium ethoxide, (5) they were heated on water-bath for 16 hours in the presence of glacial acetic acid. A few other conditions were also tried, but without success, the aldehyde and the amide being almost wholly recovered unchanged.

Condensation with n-*Butyrimide.*

n-Heptaldehyde (0·5 g.) and *n*-butyrimide (0·8 g.) were heated under different conditions: (1) heated on water-bath in the absence of any condensing agent for 16 hours, (2) heated with a trace of pyridine on water-bath for 16 hours, (3) heated for over 6 hours in the presence of pyridine-acetate: but no product could be isolated, the reactants being recovered unchanged.

Condensation with n-*Heptamide*

In the Absence of a condensing Agent.—No condensation took place when *n*-heptaldehyde (0·5 g.) and *n*-heptamide (1·2 g.) were heated (*a*) up to 16 hours on water-bath, or (*b*) up to 10 hours at 120–25° C. None took place also (*c*) in the presence of a trace of pyridine, (*d*) in the presence of pyridine-acetate, (*e*) in the presence of glacial acetic acid (130–35° C.), resinous material being sometimes obtained.

Condensation with Benzamide

1. *On a free flame with no condensing agent.*—*n*-Heptaldehyde (0·5 g.) and benzamide (1·2 g.) (1 : 2 mol.) were heated under reflux on a free flame for about 5 hours. The mixture melted, became deep yellow and syrupy but solidified on cooling. It was dissolved in boiling alcohol, and white crystalline flakes came out from the solution which were recrystallised (hot alcohol). They had the properties described by Medicus, and melted without decomposition at 128° (Medicus, 128°). N, found = 8·4, 7·96%: *n*-heptylidene-*bis*benzamide $C_{21}H_{26}N_2O_2$ required 8·28%. The yield was 0·4 g. (27·6% of theory). Medicus does not state his yield.

2. *Condensation on Water-bath without any Agent.*—Water-bath and an air-condenser were used, the heating being for 10 hours; the product was identical. The yield was slightly higher, 0·52 g. (35·9% of theory).

3. *Condensation in the Presence of a Trace of Pyridine.*—Exp. 2 was repeated with 2 drops of pyridine. Some resinification took place: the yield = 0·47 g. (32·4% of theory).

4. *Condensation at* 120–25° *without any Agent.*—Here also resinification occurred, and the yield was slightly less being 0·35 g. (24·2% of theory).

Condensation with Cinnamamide

1. *On Water-bath without any condensing Agent.*—*n*-Heptaldehyde (0·5 g.) and cinnamamide (1·5 g.) were heated without a condenser for 4 hours. The product was taken out as usual and recrystallised (hot 60% alcohol): it melted finally at 200° C. N, found: 7·3%; *n*-heptylidene-*bis*cinnamamide $C_{25}H_{30}N_2O_2$ requires 7·18%; the *mono*-amide requires 5·78%. Its properties were similar to those of the other products described above. Yield 0·75 g. (43·9% of theory).

2. *At* 120–25°, *without any condensing Agent.*—The reaction was a little quicker. Yield = 0·8 g. (46·8% of theory).

3. *In the Presence of a Trace of Pyridine.*—The three were heated (1 : 2 : 0·15 mol.) on water-bath for 10 hours; the reaction was slower and the yield less: = 0·5 g. (29·2% of theory).

Condensation with Urea

1. *On Water-bath, without a condensing Agent.*—*n*-Heptaldehyde (1·1 g.) and urea (1·3 g.) (1 : 2 mol.) were heated for 14 hours. The cold mass was crushed and washed with cold water and ether separately. The white product, having the usual properties, and recrystallised from 60% alcohol,

melted at 160°. N, found 25·8%; *n*-heptylidene-*bis*urea $C_9H_{20}N_4O_2$ requires 25·9%. The yield was 0·5 g. (or 26·3%).

2. *On Water-bath in the Presence of a Trace of Pyridine.*—The usual mol. proportions were taken. The heating was for 15 hours. The product was identical, and weighed 0·51 g. (26·8% of theory).

3. *At* 110–15° *without a condensing agent.*—After 15 hours' heating, the same product came out. Yield 0·66 g. (34·7% of theory).

4. *At* 110–15° *with a trace of pyridine.*—The yield in this case was 0·4 g. (21% of theory).

Summary

n-Heptaldehyde or œnanthaldehyde condenses with acetamide, propionamide, benzamide, cinnamamide and urea, giving fair to very good yields under particular conditions. All the products are *bis*-amides. It does not undergo condensation with formamide, *n*-butyramide and *n*-heptamide. The yields from *n*-heptaldehyde and from benzaldehyde are compared in the table above, the former giving higher yields with prioponamide and benzamide.

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GRAVIMETRIC DETERMINATION OF MANGANESE WITH 8-HYDROXY-QUINOLINE

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Berg[1] showed that manganese could be precipitated quantitatively by means of 8-hydroxy-quinoline (" Oxine ") as a dull yellow crystalline compound having the molecular formula $Mn(C_9H_6ON)_2, 2H_2O$, which was very sensitive to acids. This author suggested two methods for the precipitation. In the first method, precipitation was carried out from a hot, neutral or weakly acid solution buffered by sodium acetate and containing a small amount of sulphite or hydroxylamine, by adding an excess of an alcoholic solution of oxine. Berg (*loc cit.*) pointed out that precipitation did not occur if the solution contained 6% acetic acid and that even a slight excess of acetic acid (0·3 to 0·5%) in the presence of a large excess of sodium acetate exerted a perceptible solvent effect. In the second method, to the hot solution containing a mineral acid and an excess of an acetic acid solution of oxine but no reducing agent, ammonia was added until weakly alkaline. The same author recorded that the precipitates obtained by both the methods could not be satisfactorily dried to constant weight since at 110° C. drying was very slow and above this temperature appreciable decomposition occurred. The gravimetric determination was, therefore, carried out by this author by igniting the precipitate to the oxide, Mn_3O_4, with oxalic acid and weighing.

The conditions for the precipitation of the oxine complex have received attention from Taylor-Austin,[2] Hidehiro Goto,[3] Tsinberg[4] and Smith.[5] The importance of pH is stressed by Goto (*loc cit.*). Tsinberg (*loc cit.*) states that neither hydroxylamine nor other reducing agent is necessary for precipitating the complex even from acetic acid solutions. However, it has been tacitly assumed by all investigators following Berg that the precipitates could not be dried to constant weight. Consequently these authors either completed the determination volumetrically or ignited the complex to the tetroxide.

Raikow and Tischkov[6] have shown that the composition of the ignited tetroxide depends on the temperature and the nature of the atmosphere surrounding the precipitate during the ignition. It is obvious that this procedure is also defective in that no advantage is taken of the higher molecular weight of the oxine complex.

Although several methods for the gravimetric determination of manganese are available, it is well known that even the best among them, namely the phosphate method, requires a correction to be applied for the manganese escaping precipitation. It is, therefore, of considerable interest to re-investigate Berg's procedures.

Preliminary Investigation

In the first series of experiments the precipitations were carried out according to Berg's first procedure. Drying was found to be very slow at 110° C. and at higher temperatures marked decomposition occurred as stated by Berg. To remove adsorbed oxine alcohol was used for the final washing. On drying the precipitates in an air oven, it was found that constant weight was quickly attained even at 110° C. and no decomposition occurred at 130° C. Tests carried out on the filtrates, however, indicated the presence of manganese. Since complete precipitation of the complex occurred only at pH 5·9 (Goto, *loc cit.*) and alcohol is frequently acidic, it was concluded that washing with alcohol was not suitable though it facilitated drying. However, an important fact which emerged from these experiments is that contrary to the statement of Berg, manganese-oxine complex could be dried at much higher temperatures than 110° C. without decomposition. The present author is of opinion that a trace of manganese dioxide which may be formed under the conditions of precipitation by Berg's first method may oxidise the complex. Traces of aldehydes in the alcohol might reduce the oxide and thereby effectively prevent the decomposition. It is of interest to note in this connection that Tsinberg (*loc. cit.*) claims that no reducing agent is necessary during precipitation of manganese by oxine in acetic acid solution. Since this author ignites the precipitate to the tetroxide, the presence of manganese dioxide in the precipitate could not affect the results. A point which appears to support the above view is a fact noted by Smith (*loc. cit.*) that when a manganese solution containing both oxine and hydrogen peroxide is boiled for several minutes, a deep brown solution results. It was repeatedly observed by the present author that, when the complex was dissolved in hot dilute hydrochloric acid, a deep reddish brown solution was obtained. This seems to indicate that manganese-oxyquinolinate is readily oxidised; no such decomposition was noticed in the solution of magnesium or aluminium oxine complexes. From the above considerations it appears that to avoid decomposition of the manganese-oxine precipitates during drying it is necessary to prevent precipitation of even a trace of manganese dioxide. From the results obtained in a number of experiments, it is concluded that Berg's first method of precipitation is unsuitable if the precipitate is to be dried to constant weight. The presence of a reducing

agent during precipitation apparently did not prevent precipitation of the dioxide.

The precipitates obtained by the second method gave satisfactory results on drying without any special treatment. Prolonged drying (20 hours) at 150° C. did not produce any decomposition; even at 170° C. no decomposition occurred. At much higher temperatures a slight discoloration was occasionally noticed but it was inappreciable in amount. Even this could be avoided by adding a few drops of sulphurous acid to the solution before precipitation. However, a temperature of 150° C. was considered to be the most suitable for drying. Constant weight was attained in two to three hours and the composition of the dried precipitate corresponded to $Mn(C_9H_6ON)_2$ containing 16·03% manganese.

A series of experiments were performed to determine the best conditions for the precipitation and, as one of the objects of this investigation was to utilise the method for the determination of manganese in rock analysis, the effect of large amounts of ammonia, ammonium chloride, and sodium chloride was also investigated.

Experimental

Preparation and Standardisation of Manganese Solution

A solution of manganous chloride containing approximately 100 mg. of manganese in 50 c.c. was prepared from a pure sample of the salt. The manganese content was determined on an aliquot (50 c.c.) by conversion to and weighing as $MnSO_4, H_2O$ according to the method of Brinkmann and Smedding.[7] This method gave reproducible results and since only a pure solution of manganese was used, the figures were taken as standard. The results obtained are recorded in Table I.

Table I

No.	$MnSO_4, H_2O$ obtained	Mn calculated	Deviation from mean
			mg.
1	0·3295 g.	0·1072 g.	+ 0·2
2	0·3297	0·1072	+ 0·2
3	0·3284	0·1068	− 0·2
4	0·3289	0·1069	− 0·1

Mean value = 0·1070 g.

Oxine Reagent

A. R. quality oxine supplied by Messrs. B. D. H., London, was employed in this investigation. A 5% solution in acetic acid (2N) was prepared. This was diluted to 0·5% with the same acid when required.

Precipitation of Manganese as the Oxyquinolinate

The procedure adopted was essentially the same as the second method of Berg.

An aliquot of the manganese solution (25 c.c.) was treated with 5–15 c.c. of hydrochloric acid (2N) and a small excess (0·5 to 1 c.c.) of the oxine reagent. The solution was diluted to 100 c.c., heated to 60–70° C. and the complex precipitated by adding ammonium hydroxide (2N) from a separating funnel until the solution was distinctly alkaline to litmus. The contents were then raised to the boil and the beaker left on the water-bath for half to one hour. The precipitate was then filtered through a weighed sintered glass crucible (No. 3 porosity), washed with hot water and dried to constant weight in an air oven which was thermostatically controlled at 150° C. Constant weight was attained in two to three hours. The manganese content of the weighed precipitate was calculated on the basis of complete dehydration (16·03% Mn). Typical results obtained are given in Table II.

TABLE II

No.	Manganese (taken)	Manganese (found)	Error
1	0·0535 g.	0·0534 g.	− 0·1 mg.
2	do	0·0534	− 0·1
3	do	0·0534	− 0·1

Influence of an Excess of Oxine

Calculation shows that 53·5 mg. of manganese require approximately 6·0 c.c. of 5% oxine acetate solution. In Table III are recorded results obtained by adding a measured excess of the precipitant, the other conditions being exactly as described above.

TABLE III

(Manganese taken = 0·0535 g.)

No.	Oxine solution in excess	Manganese (found)	Error
1	2·5 c.c.	0·0536 g.	+ 0·1 mg.
2	do	0·0536	+ 0·1
3	do	0·0536	+ 0·1
4	4·5 c.c.	0·0536	+ 0·1
5	do	0·0536	+ 0·1
6	6·5 c.c.	0·0538	+ 0·3
7	do	0·0537	+ 0·2
8	9·5 c.c.	0·0541	+ 0·6
9	do	0·0541	+ 0·6
10	do	0·0540	+ 0·5

It is clear that satisfactory results are obtained in a single precipitation until nearly double the volume of reagent solution theoretically required is used and thereafter the results tend to become appreciably higher.

Double Precipitation

The first precipitation was carried out with 9·5 c.c. of the reagent in excess. The precipitate was filtered, washed and dissolved in hot hydrochloric acid (2N). A deep reddish brown solution was obtained. 1 c.c. of the reagent solution was added and the precipitation carried out with dilute ammonia as before. The results obtained are given in Table IV.

TABLE IV

No.	Manganese (taken)	Manganese (found)	Error
1	0·0535 g.	0·0540 g.	+ 0·5 mg.
2	do	0·0541	+ 0·6
3	do	0·0540	+ 0·5
4	do	0·0540	+ 0·5

Comparison of the results recorded in Tables III and IV shows clearly that when the first precipitation has been carried out with a large excess of oxine solution, the accuracy of the results could not be improved by a second precipitation. This is rather unusual and is probably connected in some manner with the production of deeply coloured solutions on dissolving the complex in acid.

Influence of Strong Ammonia

Precipitation was carried out in presence of an excess of the reagent by adding dilute ammonia and then 5 c.c. of strong ammonia (sp. gr. 0·88) was gradually added and the determination completed as before. Results obtained are recorded in Table V.

TABLE V

(Manganese taken = 0·0535 g.)

No.	Oxine solution in excess	Mn Found	Error
1	2·5 c.c.	0·0536 g.	+ 0·1 mg.
2	do	0·0536	+ 0·1
3	6·5	0·0538	+ 0·3
4	do	0·0538	+ 0·3
5	9·5	0·0549	+ 1·4
6	do	0·0548	+ 1·3

It is clear from the data recorded in the above table that when a large excess of oxine reagent is used along with strong ammonia, the values tend to be much higher than in the absence of strong ammonia.

Influence of Salts

Ammonium chloride (10 g.) or sodium chloride (15 g.) was dissolved in the manganese solution and the precipitation carried out with dilute ammonia after adding a small excess (1–2 c.c.) of the oxine reagent. The results obtained are recorded in Table VI.

TABLE VI

(Manganese taken = 0·0535 g.)

Salt added	Mn found	Error
Ammonium chloride ..	0·0535 g.	0·0 mg.
do ..	0·0536	+0·1
do ..	0·0535	0·0
Sodium chloride ..	0·0534	−0·1
do ..	0·0534	−0·1
do ..	0·0535	0·0

The results obtained show that large amounts of either ammonium chloride or sodium chloride have no influence on the accuracy.

Determination of small amounts of Manganese in presence of Sodium chloride

The solution for this determination was prepared by suitably diluting the original standardised solution. In all the cases recorded in the table below, sodium chloride (15 g.) was dissolved in the manganese solution, an excess of a 0·5% solution of oxine acetate added and the precipitation carried out exactly as described above with dilute ammonia. Finally 5 c.c. of strong ammonia was added. The precipitates were digested on the water-bath and cooled to the laboratory temperature. Experiments showed that the precipitates were finer grained than in previous cases and filtration should be carried out using No. 4 porosity sintered glass crucible. The precipitates were washed and dried as before. Typical results are recorded in Table VII.

TABLE VII

No.	Manganese (taken)	Manganese (found)	Error
1	4·0 mg.	4·1 mg.	+ 0·1 mg.
2	do	4·2	+ 0·2
3	2·7	2·7	0·0
4	do	2·8	+ 0·1
5	1·3	1·4	+ 0·1
6	do	1·4	+ 0·1
7	0·5	0·6	+ 0·1
8	do	0·6	+ 0·1
9	0·3	0·4	+ 0·1
10	do	0·4	+ 0·1

It may be noted that the conditions under which precipitations have been carried out are those which occur in the analysis of rocks if an attempt is made to precipitate magnesium and residual manganese together with oxine. Since the manganese in this mixture is determined colorimetrically, the above results should be regarded as quite satisfactory.

Summary

Precipitates of manganese oxyquinolinate obtained from a mineral acid solution containing a slight excess of oxine by adding dilute ammonia, according to Berg's second method, could be dried to constant weight at 150° C. and weighed. A slight superficial discoloration which may be observed in some cases is inappreciable even when dealing with small amounts of manganese. The composition of the dried precipitate corresponds to $Mn(C_9H_6ON)_2$ and contains 16·03% manganese.

Satisfactory results are obtained in a single precipitation provided a large excess of oxine is not added. A large excess of oxine with or without the addition of strong ammonia tends to yield higher results. Double precipitation does not improve the accuracy of the results in such cases.

The presence of large amounts of ammonium or sodium chloride does not appreciably affect the accuracy of the results.

Small amounts of manganese ranging from 0·3 to 4·0 mg. could be satisfactorily determined in presence of large amounts of sodium chloride and strong ammonia.

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2. Taylor-Austin .. *Analyst*, 1938, **63**, 571, 710
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4. Tsinberg .. *Ibid.*, 1938, **32**, 449.
5. Smith .. *Analyst*, 1939, **64**, 787.
6. Raikow and Tischkov .. *Chem. Ztg.*, 1911, **35**, 1013.
7. Brinkmann and Smedding .. *Zeit. anal. Chem.*, 1938, **114**, 161.

CONSTITUTION OF HIBISCITRIN. PART II

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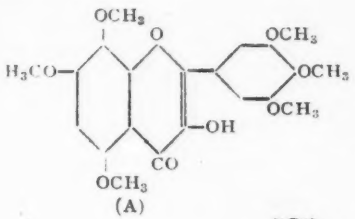
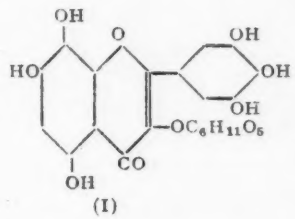
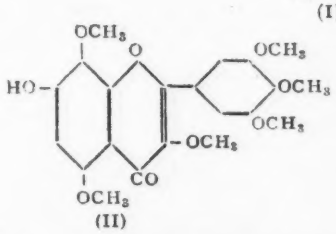
In an earlier publication (Part I[1]) it was shown that hibiscitrin is a monoglucoside of hibiscetin. It undergoes complete methylation with dimethyl sulphate and anhydrous potassium carbonate in dry acetone medium and on further hydrolysis yields O-hexamethyl-hibiscetin (A) with only one hydroxyl group free. This partial methyl ether forms trimethyl-gallic acid by fission with alkali. Hence the free hydroxyl group is not in the side phenyl nucleus. Of the other alternatives, positions 7, 8 and 5 were eliminated from considerations of melting point, colour with ferric chloride and solubility in alkali. The free hydroxyl in (A) was considered therefore to be in position 3 and thus it followed that hibiscitrin is a 3-glucoside of hibiscetin (I).



(A)



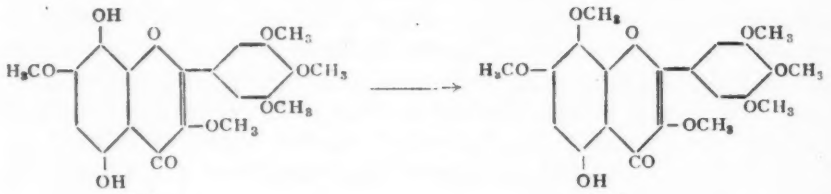
(I)



(II)

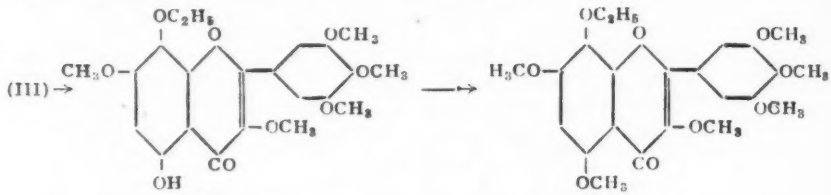
To support the above conclusion, there was need for samples of the different O-hexamethyl-hibiscetins or their derivatives for comparison with the degradation product (A) or its derivatives. The hexamethyl ether with the 7-hydroxyl alone free (II) was already known as an intermediate stage in the earlier synthesis of hibiscetin[2]; it has a much higher melting point as compared with (A) and further it does not give the ferric chloride colour. The other derivatives of hibiscetin required for the present study have now

been conveniently prepared by employing the method of nuclear oxidation in the flavone series. The synthesis of 5: 8-dihydroxy-3: 7: 3′: 4′:5′ pentamethoxy flavone (III) has been recently described by Rao and Seshadri.[3] Partial methylation of this quinol forms O-hexamethyl hibiscetin (IV) with a free hydroxyl in the 5-position. This compound crystallises from alcohol as pale lemon yellow rectangular prisms and plates and melts at 179–80°. It is sparingly soluble in aqueous alkali and gives a green colour with alcoholic ferric chloride. It is thus different from compound (A) which crystallises from alcohol as bright yellow short needles and melts at 198–200°, readily dissolves in aqueous alkali and gives a dark brown colour with ferric chloride.



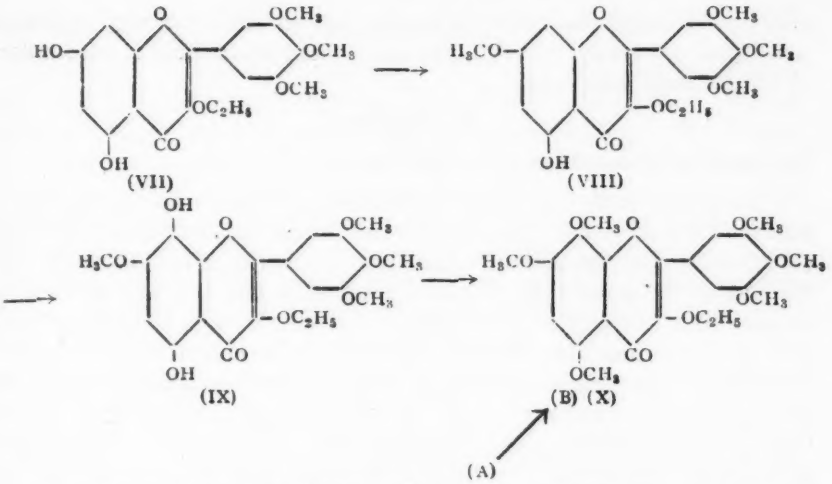
(III) (IV)

Partial ethylation of the quinol (III) and subsequent methylation produces hexamethyl-monoethyl hibiscetin (VI) with the ethoxyl in 8-position. This has a melting point of 149–50° as against 175–76° for (B), the ethyl ether of (A) and thus the two are different compounds.

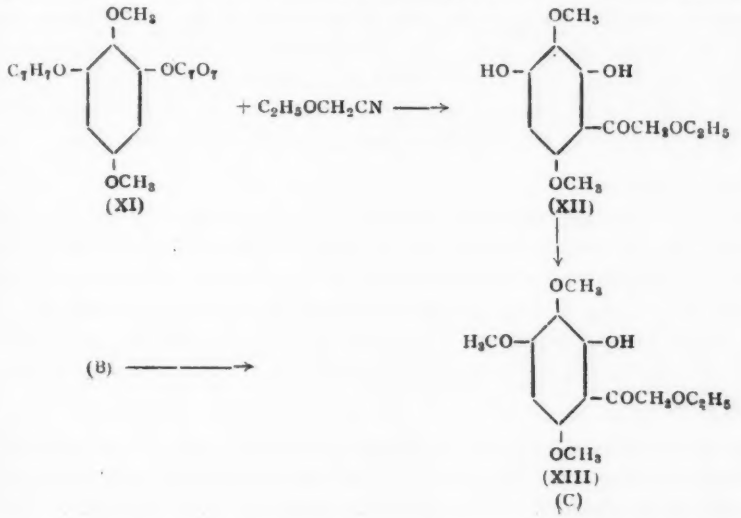


(V) (VI)

Thus all the possibilities except 3 for the position of the hydroxyl group in compound (A) are eliminated. In order to provide positive confirmation of this finding, 3-ethyl-hexamethyl hibiscetin (X) has been prepared in the following manner. Starting from ω-ethoxy-phloracetophenone[4] and trimethyl-gallic acid, 3-ethyl-3′: 4′: 5′-trimethyl ether of myricetin (VII) is obtained. This is partially methylated to form the O-tetramethyl-monoethyl myricetin (VIII) with the 5-hydroxyl free. This compound is subjected to oxidation with persulphate and the quinol (IX) fully methylated. The product (X) is found to be identical with (B) the ethyl ether of (A) derived from hibiscitrin.



In Part I it was mentioned that from the alkali fission of (A) only trimethyl gallic acid was isolated and that the ketonic product could not be obtained and characterised due to further decomposition. However its ethyl ether (B) is now found to undergo smooth fission and the ketonic part (C) could be isolated. As an independent line of evidence for the constitution of hibiscitrin, this ketone has been shown to be identical with a synthetic sample of ω-ethoxy-2-hydroxy-3 : 4 : 6-trimethoxy acetophenone



(XIII). The synthesis has been carried out in the same way as that of gossypetol-tetramethyl ether[5] except that ethoxy acetonitrile is used instead of the methoxy compound.

Experimental

Ethylation of O-hexamethyl-hibiscetin (A)

The partial methyl ether (A) of hibiscetin (1 g.) was dissolved in anhydrous acetone (50 c.c.), ethyl iodide (1 g.) and anhydrous potassium carbonate (10 g.) added and the mixture refluxed on a water-bath for 20 hours. At the end of the experiment, it was filtered while still hot and the residue washed with hot anhydrous acetone. The filtrate was concentrated and kept in an ice-chest after dilution with water. The solid that separated out was filtered and washed with dilute sodium hydroxide solution to remove any unethylated compound. The product was crystallised from alcohol when a pale brownish yellow crystalline solid was obtained. A colourless sample could be obtained by further repeated crystallisation from alcohol. The ethyl ether (B) then melted at 163–5°. When the dry substance was recrystallised from ethyl acetate, however, it readily separated out as colourless needles melting at 175–76°. (Found: C, 61·7; H, 6·2; $C_{23}H_{28}O_9$ requires C, 61·9; H, 5·8%.)

Alkali fission of ethyl ether (B)

The ethylated product (B) obtained above (0·5 g.) was boiled under reflux with absolute alcoholic potash (20 c.c., 8%) for a period of six hours. As much of alcohol as possible was then removed by distillation; the residue was dissolved in water and the solution filtered to remove any insoluble impurities. The clear solution was acidified with excess of dilute sulphuric acid and ether-extracted. The ether solution was washed three times with 5% sodium bicarbonate solution to extract the acid part.

The ketonic part (C)

The ether solution was then washed with water and on distilling off the solvent, the residue was found to be a pale yellow viscous liquid which solidified during the course of a few hours when treated with water and kept in an ice-chest. The ketone was thrice recrystallised from alcohol and it finally separated out as almost colourless flat needles melting at 135–36°. (Found: C, 57·4; H, 6·5; $C_{13}H_{16}O_6$ requires C, 57·8; and H, 6·7%.)

The acid part

The bicarbonate solution on acidification with concentrated hydrochloric acid gave rise to a precipitate which on recrystallisation from hot water was found to be identical with a synthetic sample of trimethyl gallic acid.

5-*Hydroxy*-3 : 7 : 8 : 3′ : 4′ : 5′-*hexamethoxy-flavone* (*IV*)

A solution of the 5 : 8-dihydroxy-3 : 7 : 3′ : 4′ : 5′-pentamethoxy-flavone (III)[3] (0·4 g.) in anhydrous acetone (20 c.c.) was treated with dimethyl sulphate (0·13 g.) and anhydrous potassium carbonate (5 g.). The mixture was boiled under reflux for 5 hours. At the end of the experiment the acetone was distilled off and the residue taken up with water when a light yellow solid separated out. The product was filtered and recrystallised from rectified spirits when it came out as pale lemon yellow rectangular prisms and plates melting at 179–80°. It was sparingly soluble in alkali and gave an olive green colour with alcoholic ferric chloride. (Found: C, 60·0; H, 5·0; $C_{21}H_{22}O_9$ requires C, 60·3 and H, 5·3%.)

5-*Hydroxy*-8-*ethoxy*-3 : 7 : 3′ : 4′ : 5′-*pentamethoxy-flavone* (*V*)

The dihydroxy compound (III) (0·5 g.) was dissolved in anhydrous acetone (30 c.c.) ethyl iodide (0·2 c.c.) and anhydrous potassium carbonate (5 g.) added and the mixture boiled under reflux for 5 hours. At the end of the experiment, acetone was distilled off and the residue taken up with water when the partially ethylated flavonol separated out. It was filtered and recrystallised from dilute alcohol. It came out as pale yellow rectangular plates and prisms melting at 113–15°. (Found: C, 61·3; H, 5·4; $C_{22}H_{24}O_9$ requires C, 61·1 and H, 5·6%.) The substance was sparingly soluble in alkali and gave an olive green colour with alcoholic ferric chloride.

8-*Ethoxy*-3 : 5 : 7 : 3′ : 4′ : 5′-*hexamethoxy-flavone* (*VI*)

The above compound (V) (0·4 g.) was dissolved in acetone (30 c.c.) and methylated by boiling for 30 hours with dimethyl sulphate (0·5 c.c.) and anhydrous potassium carbonate (5 g.). The solvent was then removed by distillation and the residue treated with water when the methylated product separated out. It was filtered and washed with aqueous sodium hydroxide to remove any unmethylated product. The substance was recrystallised from dilute alcohol when it came out as almost colourless (pale brown) rectangular rods tending to be needles melting at 148–50°. (Found: C, 61·6; H, 5·4; $C_{23}H_{26}O_9$ requires C, 61·9 and H, 5·8%.)

5 : 7-*Dihydroxy*-3-*ethoxy*-3′ : 4′ : 5′-trimethoxy-flavone (VII).

ω-Ethoxy-phloracetophenone (1·0 g.) was well mixed with dry trimethyl-gallic anhydride (6 g.) and dry sodium salt of trimethyl-gallic acid (3 g.). The mixture was heated at 180° for 4 hours *in vacuo*. The hard mass was then broken up and dissolved in alcohol (150 c.c.) and aqueous potassium hydroxide solution (8·0 g. in 15 c.c.) was added during the course of 20 minutes while the solution was being refluxed. The alcohol was then

completely removed under reduced pressure and the residue dissolved in water. The solution was filtered to remove impurities and the filtrate was saturated with carbon dioxide. The pale yellow compound that separated out was repeatedly crystallised from alcohol. It came out as colourless (very pale yellow) rectangular plates and rods melting at 228–30°. It gave an olive green colour with alcoholic ferric chloride. It did not exhibit any visible fluorescence in alcoholic solution. (Found: C, 61·8; H, 4·9; $C_{20}H_{20}O_8$ requires C, 61·9 and H, 5·2%.)

5-*Hydroxy*-3-*ethoxy*-7 : 3′ : 4′ : 5′-*tetramethoxy-flavone* (*VIII*)

The above 5 : 7-dihydroxy compound (VII) (1·8 g.) was partially methylated using dry acetone (50 c.c.), dimethyl sulphate (0·55 c.c.) and anhydrous potassium carbonate (5 g.) and boiling for six hours. At the end of the experiment, the acetone was distilled off and the residue treated with water when the partially methylated flavone separated out. It was very sparingly soluble in ether and also in aqueous alkali. Hence purification was effected by repeated crystallisation from a large volume of rectified spirit. It came out finally from absolute alcohol as pale yellow flat needles and narrow rectangular plates melting at 143–44°. It gave an olive green colour with alcoholic ferric chloride. (Found: C, 63·1; H, 5·3; $C_{21}H_{22}O_8$ requires C, 62·7; and H, 5·5%.)

5 : 8-*Dihydroxy*-3-*ethoxy*-7 : 3′ : 4′ : 5′-*tetramethoxy-flavone* (*IX*)

The 5-hydroxy compound (VIII) (1·4 g.) was dissolved in 20 c.c. of pyridine and aqueous potash (1·0 g. in 250 c.c. of water) was gradually added taking care to see that the solution remained clear without the separation of any precipitate. The mixture was then slowly treated with aqueous potassium persulphate (1·4 g. in 50 c.c. of water) while the mixture was kept vigorously stirred by means of an electric stirrer. The addition was completed during the course of two hours. The yellow colour of the solution gradually changed to green in the first half hour and remained deep green till the end of the experiment. After 24 hours, the solution was just acidified and filtered to remove any unreacted substance. The filtrate was also ether extracted thrice to remove the last traces. To the aqueous solution were added sodium sulphite (2·0 g.) and concentrated hydrochloric acid (25 c.c.). The mixture was then heated on a boiling water-bath for half an hour when an yellow solid separated out. This was collected by filtration and a further yield was obtained by ether extraction (total yield, 0·7 g.). The product was recrystallised from absolute alcohol from which it separated out slowly as deep yellow short needles melting at 190–92°. An alcoholic solution of the substance gave a reddish brown colour with ferric chloride. The sub-

stance dissolved in aqueous alkali to form immediately a deep red solution changing gradually to reddish violet. (Found: C, 60·4; H, 4·9; $C_{21}H_{22}O_9$ requires C, 60·3; H, 5·3%.)

3-*Ethoxy*-5 : 7 : 8 : 3′ : 4′ : 5′-*hexamethoxy-flavone* (X)

The 5 : 8-dihydroxy compound (IX) (0·5 g.) was methylated with dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (5·0 g.) in acetone solution by refluxing for a period of 25 hours. The methyl ether was crystallised from alcohol when it came out as colourless needles melting at 175–76°. (Found: C, 62·2; H, 5·6; $C_{23}H_{26}O_9$ requires C, 61·9 and H, 5·8%.) It was insoluble in alkali and did not give any colour with alcoholic ferric chloride. Mixed melting point of the substance with the mono-ethyl-hexamethyl ether of hibiscetin (B) obtained from hibiscitrin by methylation, hydrolysis and subsequent ethylation was undepressed.

2 : 4-*Dihydroxy*-3 : 6-*dimethoxy*-ω-*ethoxy-acetophenone* (*XII*)

2 : 6-Dibenzyloxy-1 : 4-dimethoxy benzene (XI) (3·5g.) prepared from pyrogallol according to the procedure adopted by Baker, Nodzu and Robinson[6] was treated with anhydrous ether (50 c.c.), dry ethoxy acetonitrile (2 c.c.) and finely powdered fused zinc chloride (1 g.). A rapid stream of dry hydrogen chloride gas was passed through the mixture for 5 hours, the reaction flask being cooled in an ice-salt mixture. The ketimine hydrochloride began to separate out as a dark brown semi-solid and the reaction was completed by keeping the flask in a refrigerator for two days. The ether was then decanted and the residue of the ketimine hydrochloride washed twice with 20 c.c. portions of dry ether. The original ether solution and the washings contained mainly benzyl chloride. The ketimine hydrochloride was dissolved in water (50 c.c.) and the solution extracted with ether to remove impurities. The hydrolysis was effected by heating the solution on the wather-bath for an hour. On cooling, the solution deposited the crude ketone as a practically colourless mass along with a small quantity of resinous matter. Further quantities could be obtained by concentration of the mother liquor and extraction with ether. The compound was soluble in sodium carbonate solution while the accompanying impurities were not. This property was made use of in the preliminary purification of the compound. It was finally crystallised from hot water when it came out as long almost colourless needles melting at 130–32°. Yield, 0·5 g. The compound was freely soluble in alcohol and dissolved with a pale yellow colour in aqueous sodium hydroxide. Its alcoholic solution developed a bluish-violet colouration with a drop of ferric chloride. (Found: C, 56·3; H, 6·3; $C_{12}H_{16}O_6$ requires C, 56·3 and H, 6·3%.)

2-Hydroxy-3 : 4 : 6-trimethoxy-ω-ethoxy-acetophenone (XIII)

A mixture of the above dihydroxy acetophenone (XII) (0·5 g.), dry acetone (25 c.c.), anhydrous potassium carbonate (5 g.) and pure dimethyl sulphate (0·3 g.) was refluxed on the water-bath for 8 hours. Acetone was then distilled off and the residue taken up with water and ether extracted. From the ether solution the partially methylated ketone was extracted by means of dilute alkali repeatedly. The combined alkali extract was acidified and then ether extracted. The solvent was distilled off from the ether extract and the residue crystallised from alcohol. The ketone came out as colourless flat needles melting at 136–37°. An alcoholic solution of the substance gave an olive green colour with ferric chloride. (Found: C, 57·4; H, 6·5; $C_{13}H_{18}O_6$ requires C, 57·8 and H, 6·7%.) The mixed melting point with ketone (C) obtained from (B) was found to be undepressed.

Summary

The constitution of hibiscitrin proposed in Part I as the 3-glucoside of hibiscetin is confirmed here by synthetic experiments. The O-hexamethyl hibiscetin (A) has been ethylated to (B). Using the method of nuclear oxidation a hexamethyl hibiscetin with a free hydroxyl in position 5 is now prepared and shown to be different from (A). Ethyl ethers of the isomeric 8- and 3-hydroxy compounds are also prepared. The former is different from (B) whereas the latter is identical with it.

Though alkali fission of (A) does not yield the ketonic part, the ethyl ether (B) can be satisfactorily employed for this fission. The ketonic product is found to be identical with ω-ethoxy-2-hydroxy-3 : 4 : 6-trimethoxy-acetophenone obtained synthetically, thus confirming again the above constitution of (B) and of hibiscitrin.

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2. Rao, Rao and Seshadri .. *Ibid.*, A, 1944, **19**, 88.
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NUCLEAR OXIDATION IN THE FLAVONE SERIES

Part XI. A New Synthesis of Nobiletin

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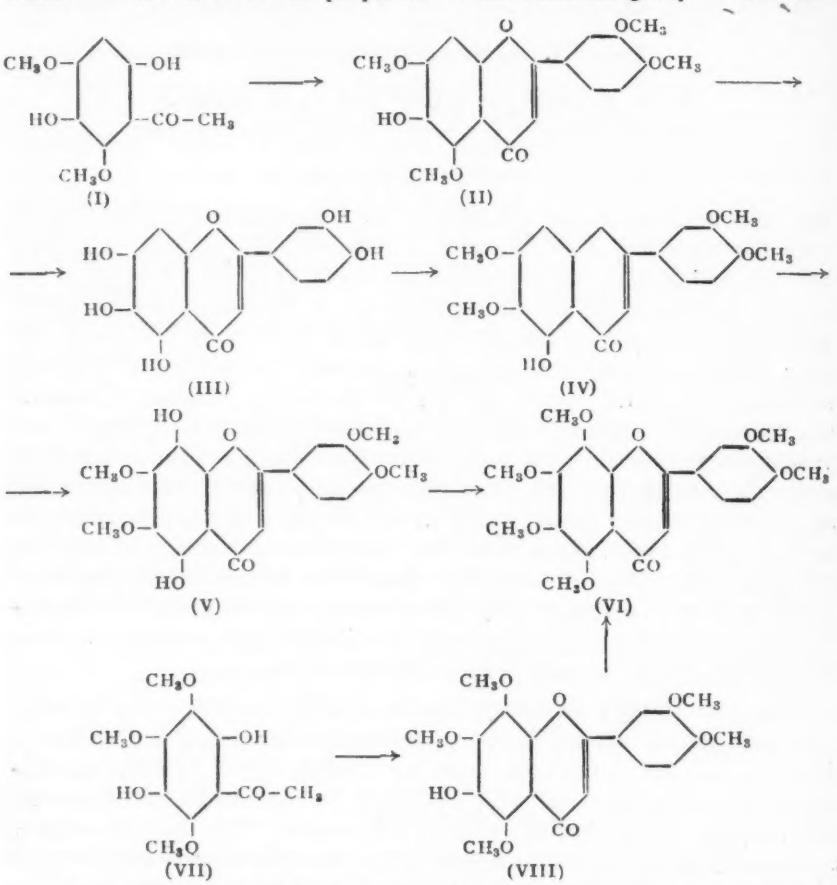
The experiments on nuclear oxidation in the flavone series published recently from this laboratory are important in three different respects. (1) They have effected considerable simplification in the synthesis of many of the flavones and flavonols; (2) the establishment of the constitution of flavone derivatives such as glycosides and methyl ethers has been rendered easier and more definite; (3) they serve as model experiments for schemes of biogenesis of the members of this group. In Part VII[1] the nuclear oxidation of baicalein and scutellarein leading to the preparation of 6:8-dihydroxy-chrysin and 6:8-dihydroxy-apigenin and their derivatives was described. But these compounds have not so far been found to occur in nature. The well-known representative of this group of flavones having hydroxyl groups in all the four positions 5:6:7:8, is nobiletin[2] which is the hexamethyl ether of 6:8-dihydroxyluteolin. It was first synthesised by Horii[3] starting from 2-hydroxy-3:4:5:6-tetramethoxy-acetophenone and adopting the Baker-Venkatraman method. The synthesis of nobiletin and nornobiletin using the method of nuclear oxidation is described in this paper.

For this synthesis 6-hydroxy-luteolin, a higher member of the baicalein series of flavones was required. It has not so far been described in the literature and has now been made by condensing 2:5-dihydroxy:4:6-dimethoxy acetophenone (I)[4] with the anhydride and sodium salt of veratric acid adopting the method of Allan and Robinson. This method which is so eminently successful in the synthesis of the flavonols offers some difficulties when applied to flavones and hence alternative methods like that of Baker and Venkatraman have been sought to be used. One of the main difficulties is acylation in the 3-position which is now realised to take place invariably in this condensation. But it is our experience that the 3-acyl group could be conveniently removed by boiling with aqueous sodium carbonate without complications from other decompositions. Using this extra step the method is capable of much wider use in the case of flavones also. In the particular example under consideration there was also partial demethylation in the 5-position leading to a mixture. Instead of attempting to

separate it, it was directly demethylated to yield 6-hydroxy-luteolin (III) which exhibits all the characteristic properties of the baicalein group of flavones.



As in other cases of nuclear oxidation, preliminary partial methylation of (III) was effected forming the 6:7:3′:4′-tetramethyl ether (IV) leaving the 5-hydroxyl free. Oxidation with alkaline persulphate proceeded smoothly and yielded the quinol (V). Subsequent methylation produced nobiletin (VI) and demethylation nor-nobiletin. These products had all the properties and reactions described in the literature.

As a check the synthesis of nobiletin starting from 2:5-dihydroxy-3:4:6-trimethoxyacetophenone (VII)[5] and condensing directly with sodium veratrate and veratric anhydride has also been carried out. Even here the

6-hydroxy-compound (VIII) could not be obtained pure due to partial demethylation in the course of the condensation. But fairly satisfactory yields of nobiletin could be obtained by methylating the mixture. This procedure appears to be more convenient than that adopted by Horii.[3]

Experimental

Condensation of 2 : 5-*Dihydroxy*-4 : 6-*dimethoxy-acetophenone* (I) *with veratric anhydride and sodium veratrate*

The ketone[4] (2 g.) was intimately mixed with veratric anhydride (10 g.) and sodium veratrate (3 g.) and heated in an oil-bath at 180° for 4 hours under vacuum. The hard mass was then broken up and refluxed with 10% alcoholic potash for half an hour. The alcohol was removed under reduced pressure, the residue dissolved in water and the reddish-brown solution saturated with carbon dioxide. The precipitated flavone was extracted with ether, the ether solution was dried over anhydrous sodium sulphate and the solvent distilled off. The bright yellow solid was boiled with 5% aqueous sodium carbonate for ½ hour to hydrolyse the 3-acyl group and then the clear solution acidified and the precipitate recrystallised from rectified spirit; yield, 0·7 g. It was found to have a melting point ranging from 190° to 206° and was therefore considered to be a mixture of the 6-hydroxy (II) and the 5 : 6-dihydroxy flavone derivatives; this was supported by its colour with ferric chloride. The mixture was used directly for demethylation. It dissolved in alkali to a bright yellow solution and gave a brown colour with ferric chloride in alcoholic solution.

5 : 6 : 7 : 3′ : 4′-*Pentahydroxy-flavone* (*III*)

The mixture of the 6-hydroxy and the 5 : 6-dihydroxy compounds obtained above (0·6 g.) was dissolved in acetic anhydride (15 c.c.) and to the solution was added hydriodic acid (d. 1·7; 15 c.c.) cautiously with cooling. The solution was refluxed gently for 1 hour and then diluted with aqueous sulphur dioxide solution. The precipitated hydroxy-flavone was filtered off and washed thoroughly with sulphur dioxide water and finally with water. It was dried and recrystallised from dry ethyl acetate when it was obtained as a bright yellow solid appearing as yellow rectangular plates under the microscope and melting at 315° with decomposition. Yield 0·4 g. (Found: C, 59·2; H, 3·6; $C_{15}H_{10}O_7$ requires C, 59·6 and H, 3·3%.)

The pentahydroxy flavone gave with ferric chloride a brown colour in alcoholic solution. With sodium bicarbonate solution the compound quickly dissolved giving a transient green colour to the solution which rapidly changed into brown. With aqueous sodium carbonate and sodium hydroxide, it

gave brown solutions. The compound responded to Bargellini's test; there was an immediate precipitation of green flocks on adding sodium amalgam to an alcoholic solution, the solution itself remaining yellowish-brown.

5-*Hydroxy*-6 : 7 : 3′ : 4′-*tetramethoxy-flavone* (*IV*)

The above pentahydroxy-flavone (0·6 g.) was dissolved in anhydrous acetone (50 c.c.) and to the solution were added redistilled dimethyl sulphate (1·2 c.c.) and freshly ignited potassium carbonate (6 g.). The mixture was refluxed on a water-bath for a period of 6 hours at the end of which the solution was filtered and evaporated. The 5-hydroxy compound was obtained as a yellow solid and was purified by recrystallisation from rectified spirit; yield 0·4 g. It appeared as yellow rectangular prisms and rods under the microscope and melted at 223–4°. (Found: C, 63·3; H, 5·2; $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%). The substance dissolves to a bright yellow solution in sodium hydroxide and gives a brown colour with ferric chloride in alcoholic solution.

5 : 6 : 7 : 3′ : 4′-*Pentamethoxy-flavone*

The mixture of the compounds obtained from the Allan-Robinson condensation (0·2 g.) was methylated with dimethyl sulphate (0·5 c.c.) and anhydrous potassium carbonate (2 g.) in anhydrous acetone medium by refluxing for 30 hours. The acetone solution was then filtered and evaporated and the colourless solid was purified by recrystallisation from rectified spirit when it appeared as colourless long rectangular plates and needles and melted at 142–3°. Yield 0·1 g. (Found: C, 63·1; H, 5·8; $C_{20}H_{20}O_7$, $\frac{1}{2}$ H_2O requires C, 63·0; H, 5·5%.)

It gave bright yellow solutions with concentrated hydrochloric and sulphuric acids and developed a red colour on reduction with magnesium powder and hydrochloric acid in an alcoholic solution.

5 : 8-*Dihydroxy*-6 : 7 : 3′ : 4′-*tetramethoxy-flavone* (*V*)

To a stirred solution of 5-hydroxy-6 : 7 : 3′ : 4′-tetramethoxy-flavone (IV) (0·5 g.) dissolved in a mixture of pyridine (10 c.c.) and aqueous sodium hydroxide (2 g. in 20 c.c. of water) was added a solution of potassium persulphate (2 g. in 50 c.c. of water) during a period of 2 hours. The mixture was stirred for another hour more and the deep red solution was allowed to stand for 24 hours. It was then just acidified with hydrochloric acid and the unreacted 5-hydroxy compound filtered and the last traces removed by extracting the filtrate with ether. 15 c.c. of strong hydrochloric acid was then added to the aqueous solution and heated in a boiling water-bath for $\frac{1}{2}$ hour. After cooling, the solution was extracted repeatedly with ether and the

ether solution dried over anhydrous sodium sulphate and the solvent distilled off. The orange yellow solid recrystallised from alcohol when it was obtained as golden yellow broad rectangular plates melting at 212–13°. Yield 0·2 g. (Found: C, 61·2; H, 5·1; $C_{19}H_{18}O_8$ requires C, 60·9 and H, 4·8%).

The compound dissolves to an orange red solution in sodium hydroxide; it gives a deep brown-red colour with ferric chloride in alcoholic solution and the colour becomes darker on adding excess of the reagent.

5:6:7:8:3′:4′-*Hexamethoxy-flavone* (*Nobiletin*) (*VI*)

The above 5:8-dihydroxy-compound (0·2 g.) was methylated with redistilled dimethyl sulphate (1·0 c.c.) and anhydrous potassium carbonate (2 g.) in dry acetone solution by refluxing for a period of 30 hours. The acetone solution was filtered off and the inorganic salts washed with a little acetone. On distilling off the solvent a pale yellow solid was obtained which was recrystallised from dry ethyl acetate. Nobiletin was obtained as pale yellow elongated rectangular prisms and needles melting sharp at 129–30°. (Found: C, 62·6; H, 5·4; $C_{21}H_{22}O_8$ requires C, 62·7 and H, 5·5%.)

The synthetic compound had all the properties of the natural specimen as described by Robinson and Tseng.[2] The mixed melting point with the compound obtained by the Allan-Robinson method (described later) was undepressed.

Nornobiletin

Nobiletin (0·2 g.) was dissolved in acetic anhydride (4 c.c.) and cautiously treated with hydriodic acid (4 c.c., d., 1·7) with cooling. The dark red solution was refluxed for 30 minutes at 145° (oil-bath) and then poured into ice-water. The liberated iodine was decomposed by means of sulphur dioxide and the precipitated hydroxy-flavone filtered and dried. It was recrystallised from a large excess of absolute alcohol when nornobiletin was obtained as deep yellow rectangular prisms, melting with decomposition at 310–12°. Yield 0·12 g. The compound was also soluble in boiling ethyl acetate and gave all the colour reactions recorded in the literature.[2]

Condensation of 2:5-*dihydroxy*-3:4:6-*trimethoxy acetophenone with veratric anhydride and sodium veratrate*

A mixture of the ketone[5] (2 g.), veratric anhydride (10 g.) and sodium veratrate (4 g.) was heated in an oil-bath at 180° for 4 hours under vacuum. At the end of this operation, the solid was suspended in alcohol (50 c.c.) and refluxed for 30 minutes after the addition of an alcoholic solution of potassium hydroxide (4 g. in 10 c.c.). The alcohol was removed under

reduced pressure, the residue dissolved in water and filtered. The filtrate was saturated with carbon dioxide and the precipitated flavone extracted with ether. After the removal of the ether, a yellow oil was obtained which did not solidify even after it was kept in the ice-box for 2 days. It was then boiled with 5% aqueous sodium carbonate for ½ hour. Even then the product did not turn into a solid. It gave a brownish-green colour with an alcoholic solution of ferric chloride and seemed to be a mixture containing some partially demethylated product (5: 6-dihydroxy-compound) also. It was therefore directly used for methylation.

5: 6: 7: 8: 3′: 4′-*Hexamethoxy-flavone* (*Nobiletin*) (*VI*)

A solution of the above product in dry acetone (30 c.c.) was treated with dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (5 g.). The mixture was refluxed on a water-bath for 20 hours and at the end of this period the acetone solution was filtered off and the residue washed with hot acetone. On removal of the solvent, a yellow oil was obtained which soon solidified to a pale yellow solid. Purification was effected by recrystallisation from ethyl acetate when nobiletin was obtained as pale yellow rectangular prisms melting sharp at 130–31°. It did not dissolve in alkali and gave no colour with alcoholic ferric chloride. The mixed melting point with the sample obtained by the method of nuclear oxidation was not depressed.

Summary

Nobiletin has been synthesised by adopting the method of nuclear oxidation of the flavone skeleton. For this purpose 6-hydroxyluteolin has been prepared for the first time and subjected to partial methylation, oxidation and final methylation successively whereby nobiletin is obtained. Demethylation of this yields nornobiletin having all the propertics described in the literature. Nobiletin has also been prepared independently from 2: 5-dihydroxy-3: 4: 6-trimethoxy-acetophenone by condensation with sodium veratrate and veratric anhydride and subsequent methylation.

References

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2. Robinson and Tseng .. *J. C. S.*, 1938, 1004.
3. Horii .. *Bri. Chem. Abs.*, 1941, A, II, 331.
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5. Baker .. *J. C. S.*, 1941, 666.

A NEW EFFECT OF HYDROGEN BOND FORMATION

Chelation and Stability of Flavanones

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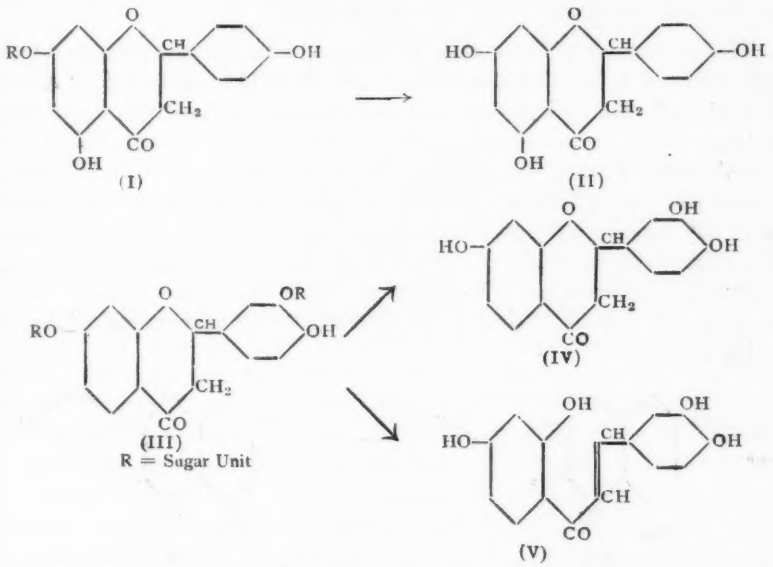
In the course of the study of the flavanone glycosides, naringin[1] (I) and butrin[2] (III), a remarkable difference was noticed in their behaviour when subjected to acid hydrolysis; whereas the former yields a single aglucone, naringenin (II) which gives all the reactions for a flavanone, the latter under the same conditions forms a mixture of aglucones which could be separated by employing their difference in solubility in water. It consists of the flavanone, butin (IV) and the chalkone, butein (V).

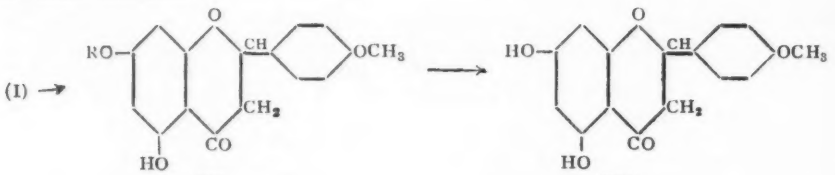


In order to make sure of the individual nature of each product and its freedom from admixture, the following characteristic colour tests have been employed besides the usual criteria of purity based on crystal structure and melting point. The colour reaction (bright red and allied colours) with magnesium and hydrochloric acid in an alcoholic solution is positive for

flavanones and is not given by the isomeric chalkones. On the other hand the chalkones give a positive boric-citric[3] reaction which is negative for the flavanones. Using a combination of these the aglucone obtained by the hydrolysis of naringin is found to be an unmixed flavanone (naringenin) and butrin yields a mixture as already stated.

A similar difference in behaviour is exhibited by the two isomeric flavanones, butin and naringenin when heated with mineral acids or dissolved in alkali and reprecipitated by acids; the former undergoes partial change into the chalkone, butein whereas the latter is unaffected. This phenomenon, *i.e.*, the difference in the stability of the flavanone ring as found in naringin and naringenin on the one hand and butrin and butin on the other should be capable of explanation based on the structures of these compounds. The apparent difference that could be directly noticed is the presence of a 5-hydroxyl group in naringin and naringenin and its absence in butrin and butin and this could be considered to be mainly responsible. This surmise is supported by the following experiments in the partial methylation of naringin and naringenin using dimethyl sulphate.

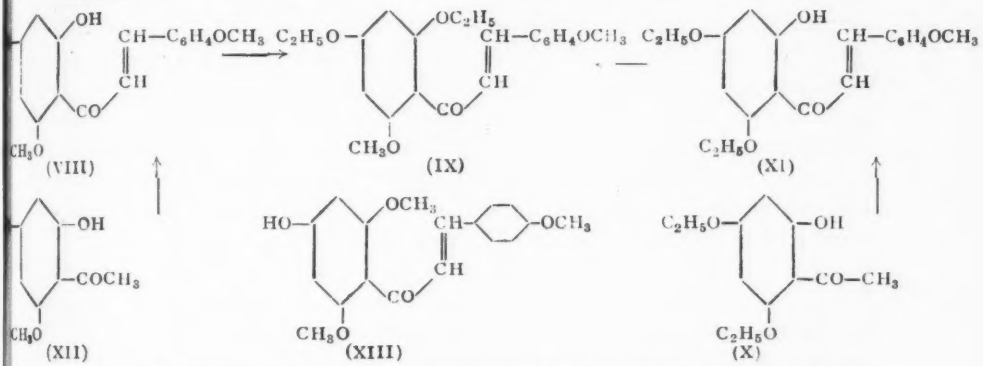
That naringin is a 7-glycoside of naringenin has already been mentioned. Methylation of it using diazomethane was originally investigated by Asahina and Inubuse.[4] He noticed that only one methyl group entered the molecule and when the product was hydrolysed it yielded isosakuranetin (VII) which is the 4′-methyl ether of naringenin. The same result has now been obtained by using just one molecular proportion of dimethyl sulphate for the methylation in dry acetone solution in the presence of anhydrous potassium carbonate as the condensing agent. The final product of hydrolysis (isosakuranetin) gives all the reactions of a flavanone and is free from chalkone. Again it is stable to cold alkali since it is recovered unchanged on acidifying the alkaline solution.



(VI) (VII)

But on methylation using two mols. of dimethyl sulphate, the hydroxyl in the 5-position is also methylated and when the glycoside dimethyl ether is hydrolysed the product is found to consist of 2:4-dihydroxy-6:4′-dimethoxy chalkone (VIII). The constitution of this chalkone has now been established in two ways. (1) It is ethylated and the diethyl ether shown to

be identical with a synthetic sample of 2:4-diethoxy-6:4′-dimethoxy-chalkone (IX). The latter has now been synthesised from phloracetophenone-diethyl ether (X) by first condensing it with anisic aldehyde and finally methylating the chalkone (XI). (2) The dihydroxy chalkone (VIII) has itself been synthesised in the following manner and direct comparison effected. The mono-methyl ether of phloracetophenone (XII) is prepared for this purpose by the partial demethylation of the trimethyl ether according to the method of Gulati and Venkatraman[5] and condensed with anisaldehyde.

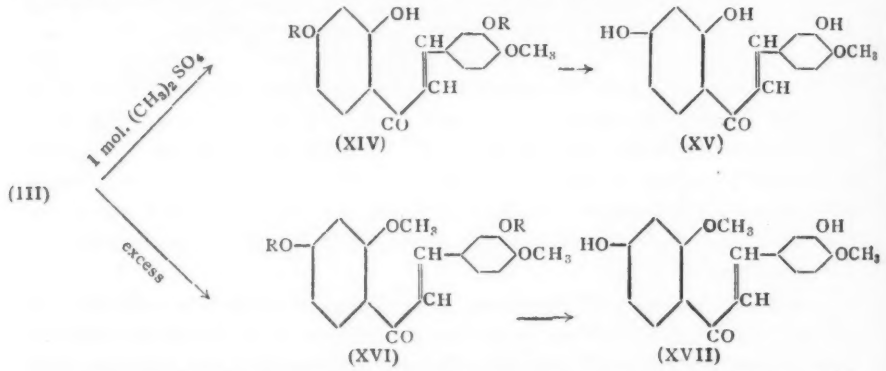


In this connection could be mentioned the work of Sonn and Bülow[6] who condensed acetonitrile with the monomethyl ether of phloroglucinol. The ketone thus obtained was provisionally given the structure 6-methoxy-2:4-dihydroxyacetophenone. This underwent smooth condensation with anisaldehyde to a chalkone melting at 169° which was given provisionally the constitution of 4′:6-dimethoxy-2:4-dihydroxychalkone. The properties of this compound agreed closely with the dimethyl ether (VIII) described above and thus the tentative constitution given by Sonn and Bülow for their product is shown to be correct. Using methoxy-acetonitrile and phloroglucinol-monomethyl ether, more recently Kuhn *et al.*[7] obtained ω:6-dimethyl-ether of phloracetophenone. This further supports Sonn and Bülow's constitution for their acetophenone derivative and chalkone. Obviously in these reactions the monomethyl ether of phloroglucinol behaves like resorcinol.

Methylation of naringin using three mols. of dimethyl sulphate and subsequent hydrolysis leads to the formation of 2:6:4′-trimethoxy-4-hydroxy-chalkone (XIII). In this case the third methyl group has entered after the flavanone ring opened out. The chalkone is found to be identical with a synthetic sample prepared by Rangaswami and Seshadri.[1] From

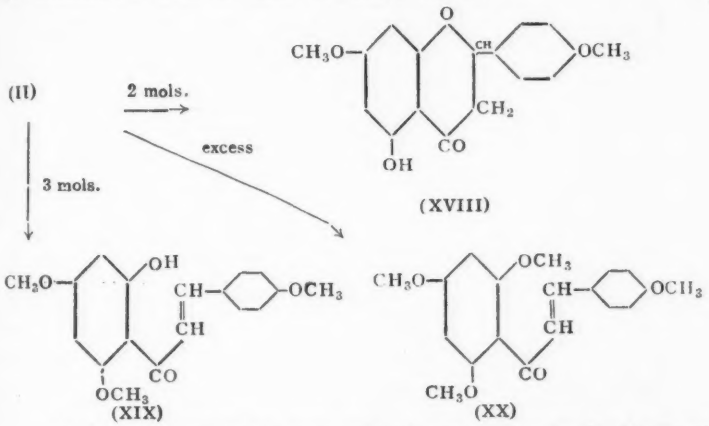
the experiments described above it will be clear that the methylation of the 5-hydroxyl affects the stability of the flavanone ring markedly and the corresponding chalkone is obtained as the product. It is possible that mixtures of chalkones and flavanones are produced in these reactions but the presence of the latter could not be detected by qualitative tests.

The methylation of butrin was effected earlier by Rao and Seshadri[3] using diazomethane. Under the mild conditions employed the free hydroxyl alone was methylated without any further change and the monomethyl ether was obtained fully in the flavanone form. It was colourless and it melted at 226–28°. Reichel *et al.*[8] later reported its synthesis and the melting point of the synthetic product given by them agrees with that noted earlier for methyl-butrin. In order to get information about the behaviour of butrin under the conditions of methylation now adopted for naringin, fresh experiments have now been conducted. Though butrin is only sparingly soluble in acetone a fine suspension of it in this solvent reacts with dimethyl sulphate and potassium carbonate. With one mol. of dimethyl sulphate a monomethyl ether is formed; but it is different from the one already described. It melts at 190° and has the properties of 2-hydroxy-4: 3′-diglucosidoxy-4′-methoxy chalkone (XIV) prepared synthetically by Reichel *et al.*[8] Thus the flavanone ring gets opened out during this methylation. On hydrolysis the new methyl ether yields a monomethyl butein (XV) which is found to be identical with a synthetic sample of 4′-methyl butein. With two mols. or excess of dimethyl sulphate butrin forms a dimethyl ether (XVI). This on hydrolysis produces a dimethyl butein (XVII) found to be identical with a synthetic sample of 2: 4′-dimethoxy-4: 3′-dihydroxy chalkone.



The special importance of the 5-hydroxyl group for the stability of the flavanone structure is again confirmed by methylation experiments using

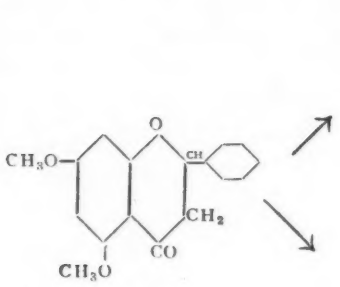
naringenin (II) itself. Shinoda and Sato[9] reported that they could obtain sakuranetin (7-methyl ether of naringenin) by using one molecular proportion of diazomethane. This result could not be obtained now by using one mol. of dimethyl sulphate. A mixture results and though it is found to consist only of flavanones, it could not be separated. However when two mols. of dimethyl sulphate are employed a definite compound, 7 : 4′-dimethoxy-5-hydroxy-flavanone (XVIII) (sakuranetin-methyl ether) is formed. This was obtained earlier by a number of workers, (1) by the methylation of sakuranetin with diazomethane (Asahina and Inubuse[4]), (2) by the methylation of isosakuranetin (Hattori[10]) and (3) by the methylation of naringenin itself using excess of diazomethane (Shinoda and Sato[9]). Geissman and Clinton[11] prepared the same compound by methylating naringenin with dimethyl sulphate and potash in methyl alcoholic solution. They could separate a small quantity of naringenin-4′-methyl ether (isosakuranetin) as a by-product. The dimethyl ether gives all the properties of a flavanone, can be recovered from an alkaline solution by acidification and is stable to boiling dilute acid. On the other hand with 3 mols. or excess of the methylating agent the chalkone tri-(XIX) and tetramethyl (XX) ethers are formed. These were identified by comparison with authentic samples synthetically obtained by the condensation of anisaldehyde with phloracetophenone di- and trimethyl ethers.[12]



Methylation of butin was carried out earlier by Perkin and Hummel[13] using aqueous alkali and dimethyl sulphate. They obtained a mixture of butin and butein trimethyl ethers. This reaction has now been examined using potassium carbonate and dimethyl sulphate. It has not been found possible to effect partial methylation using one and two mols. of the reagent and isolate definite products. With three mols., butein 4 : 3′ : 4′-trimethyl

ether is readily obtained and with four mols. and excess butein tetramethyl ether. These have been characterised by comparison with synthetic samples.

A few simpler compounds have also been tested for their stability to acid and alkali. 7-Methoxy-5-hydroxy-flavanone[13] (XXII), 5:7-dihydroxy-flavanone (XXIII) and 5-hydroxy-flavanone (XXIV) belong to one category. The first two have been obtained by the partial and complete demethylation of 5:7-dimethoxy flavanone (XXI) using aluminium chloride and the last prepared for the first time by a similar demethylation of 5-methoxy-flavanone.[19]



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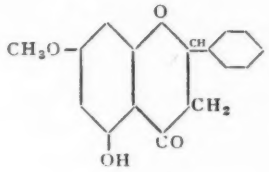

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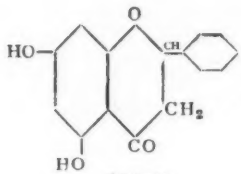
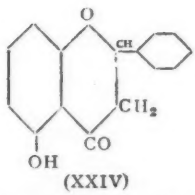


(XXIII)



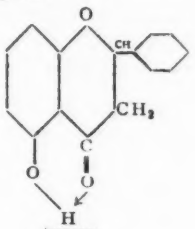
(XXIV)

All the three are found to be stable. On the other hand the methyl ethers, 5-methoxy-flavanone and 5:7-dimethoxy-flavanone (XXI) are unstable.

An interesting observation made in the past which is relevant to the present theme relates to the synthesis of polyhydroxy chalkones by the condensation of cinnamoyl chloride and its derivatives with polyhydroxy phenols in nitrobenzene solution using aluminium chloride as the condensing agent. It was observed by Shinoda and Sato[14] that when resorcinol was used the main products were chalkone derivatives whereas with phloroglucinol mainly flavanone derivatives were obtained. In the latter case the chalkones are unstable and by heating with glacial acetic acid or by heating

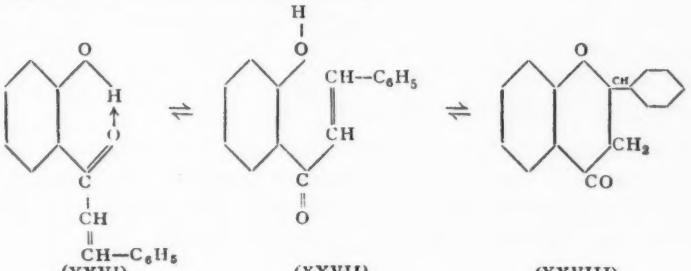
above their melting points they change over to flavanones. Employing the ethyl carbonate of *p*-hydroxy-cinnamic acid the above authors[14] and also Rosenmund[15] synthetically obtained the flavanone, naringenin by the above method. It may further be mentioned here that whereas with resorcinol derivatives like butrin the corresponding chalkone (butein) has also been found to occur in nature,[16] in the case of phloroglucinol derivatives only flavanones are found and the corresponding chalkones do not appear to have been isolated from natural products so far. The presence of a free 5-hydroxyl group may account for this feature and the flavanones concerned should have greater stability.

The above-mentioned significant influence of the 5-hydroxyl group is capable of being explained on the basis of the existence of a hydrogen bond (chelation) involving this hydroxyl and the neighbouring carbonyl group which contributes to the stability of the flavanone structure. That chelation exists in 5-hydroxy-flavanones (XXV) is established by the characteristic colour reactions and the resistance offered to the methylation of this hydroxyl group by mild methylating agents.



(XXV)

In order to explain clearly the part played by the chelation it is necessary to understand the flavanone-chalkone relationship and interconversion in detail. In simple cases it is known that chalkones and the corresponding flavanones exist in equilibrium in an acid or alkaline medium and hence there is certain amount of stability associated with each structure. The following may represent the relationship.



(XXVI) (XXVII) (XXVIII)

That chalkones are largely chelated is amply borne out by their properties and thus structure (XXVI) will correctly represent them. The existence of the non-chelate form (XXVII) though in small amounts in ortho-hydroxy-carbonyl compounds is revealed by the Raman Effect.[18] This was originally explained by giving the trans-structure to the OH group alone. It seems to be more correct to consider that the moving apart of the CO group is also involved as shown in (XXVII).

The presence of a 5-hydroxyl adds more stability to the flavanone structure by the formation of an additional chelate ring as shown in (XXV). Even if the flavanone ring opens the concerned groups are not able to move far enough to yield a stable chalkone. On the other hand whatever alternative constitution the chalkone takes in this case it is favourable for quick conversion into the flavanone. As soon as the 5-hydroxyl is methylated this influence vanishes and the normal conversion into a stable chalkone becomes possible.

Experimental

Hydrolysis of naringin

Naringin was boiled with dilute sulphuric acid (7%) It readily went into solution and after half an hour the aglucone separated out. After heating for 2 hours the solid was filtered off and crystallised from alcohol. It was quite colourless and melted at 243–44°. An alcoholic solution gave a bright red colour with magnesium and hydrochloric acid. No yellow colour was produced with boric and citric acids in dry acetone solution and thus the test for chalkone was negative.

Methylation of naringin

(*a*) *Using one mol. of dimethyl sulphate.*—A solution of naringin (2 g.) in dry acetone (30 c.c.) was refluxed with dimethyl sulphate (0·35 c.c., 1 mol.) and anhydrous potassium carbonate (3 g.) for 20 hours. The potassium salts were then separated by filtration and washed with warm acetone. The acetone filtrate was evaporated when an oily residue was obtained. It did not solidify even after 24 hours. It was, therefore, refluxed with 7% sulphuric acid for two hours. The liquid was cooled and extracted with ether. The ethereal extract was dried over calcium chloride and evaporated. A colourless crystalline solid was obtained. It crystallised from alcohol in the form of colourless tiny prisms, melting at 187–89°.

The potassium salts were dissolved in water, acidified with sulphuric acid and refluxed for two hours. When the resulting liquid was extracted with ether and the ether extract evaporated a small quantity of the above compound was obtained. Total yield, 0·5 g.

It gave reddish brown colour with alcoholic ferric chloride and blue colour with concentrated sulphuric acid.[10] When reduced with magnesium and hydrochloric acid the alcoholic solution was scarlet red. No colour was developed in the boric-citric acid test. It was found to be identical with isosakuranetin (VII).[4]

(*b*) *Using two mols. of dimethyl sulphate.*—The above experiment was repeated with naringin (2 g.) and two molecular proportions of dimethyl sulphate (0·7 c.c.). When the acetone solution was evaporated, an oily residue was obtained. It was hydrolysed by refluxing with 7% sulphuric acid for two hours. The liquid was ether-extracted and the ether removed by evaporation. When the yellow solid residue was crystallised from ethyl acetate, it was obtained in the form of yellow prisms and needles melting at 165–67°. A small quantity of the same compound was also recovered from the potassium salts after boiling with aqueous acid. Total yield, 0·5 g.

It gave a brown colour with ferric chloride in alcoholic solution but developed no colour with magnesium and hydrochloric acid. It was soluble in aqueous sodium hydroxide yielding an yellow solution and dissolved in sulphuric acid with red colour. A mixed melting point determination with a synthetic sample of 2:4-dihydroxy-6:4′-dimethoxy chalkone (VIII) described below showed no depression.

Ethyl derivative.—The above product (0·2 g.) was dissolved in dry acetone (20 c.c.) and ethyl iodide (1 c.c.) and anhydrous potassium carbonate (3 g.) were added. The mixture was refluxed for 20 hours. The solvent was then removed by evaporation and water added to the residue when a yellow crystalline solid separated out. It was filtered and crystallised from a mixture of ethyl acetate and alcohol when it came out as pale yellow broad rectangular plates melting at 120–22°. A mixed melting point determination with a synthetic sample of 6:4′-dimethoxy-2:4-diethoxy-chalkone (IX) described later on showed no depression.

(*c*) *Using excess of dimethyl sulphate.*—Naringin (2 g.) was methylated as before with excess of dimethyl sulphate (2 c.c.). The residue obtained after evaporating the acetone solution was hydrolysed by refluxing with 7% sulphuric acid for 2 hours. On cooling, a yellow crystalline solid separated. It was collected and crystallised from alcohol when it came out in the form of pale yellow needles and micaceous plates melting at 202–4°. A small quantity of the same compound could also be recovered from the potassium salts. It developed no colour with ferric chloride in alcoholic solution and dissolved in aqueous sodium hydroxide yielding an yellow solution. Its melting point was not depressed when mixed with a synthetic sample of 2:6:4′-trimethoxy-4-hydroxy chalkone[1] (XIII).

Synthesis of 2:4-*dihydroxy*-6:4′-*dimethoxy-chalkone* (*VIII*).—To a solution of 2:4-dihydroxy-6-methoxy acetophenone (0·5 g.) and anisaldehyde (2 c.c.) in alcohol (20 c.c.) was added potassium hydroxide (2 g. in 2 c.c. of water) little by little with shaking. More alcohol was added to obtain a clear solution and the container was corked air-tight and left aside for 60 hours. The solution was then diluted with a large amount of water and extracted with ether to remove any unreacted aldehyde. The remaining aqueous solution on acidification deposited a bright yellow oil which was taken up in ether. The ethereal extract was washed with dilute sodium bicarbonate solution to remove any free anisic acid. On evaporating the ether, a yellow crystalline solid was obtained which was again crystallised from alcohol. The chalkone was thus obtained as yellow prisms and needles melting at 165–7°. Yield, 0·2 g. (Found: C, 67·8; H, 5·6; $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·3%.)

2-*Hydroxy*-4′-*methoxy*-4:6-*diethoxy chalkone* (*XI*)

4:6-Diethoxy-2-hydroxy-acetophenone (X) obtained by the partial ethylation of phloroacetophenone (1 g.) and anisaldehyde (5 c.c.) were dissolved in alcohol and potassium hydroxide (8 g. in 8 c.c. of water) added to it little by little with shaking. The condensation was carried out as given above. The crude product separated as a yellow solid; it was filtered and washed with sodium bicarbonate solution to remove any anisic acid and then crystallised from alcohol. The chalkone was thus obtained in the form of bright yellow rectangular plates melting at 110–12°. Yield, 1 g. (Found: C, 70·6; H. 6·6; $C_{20}H_{22}O_5$ requires C, 70·2 and H, 6·4%.)

2:4′-*Dimethoxy*-4:6-*diethoxy-chalkone* (*IX*)

The above chalkone (0·5 g.) was methylated in anhydrous acetone medium with dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (2 g.). After refluxing the mixture for 15 hours, the solvent was removed by distillation and water added to the residue. The yellow solid that separated out was filtered, washed and crystallised from a mixture of ethyl acetate and alcohol. It was obtained as lemon yellow broad rectangular plates melting at 120–22°. Yield, 0·4 g. The chalkone was insoluble in alkali and sparingly soluble in alcohol. It gave no colour with ferric chloride in alcoholic solution. (Found: C, 70·4; H, 7·0; $C_{21}H_{24}O_5$ requires C, 70·8; and H, 6·7%).

Methylation of butrin

(*a*) *With* 1 *mol. of dimethyl sulphate*.—Butrin (1 g.) was finely powdered and suspended in dry acetone (40 c.c.), dimethyl sulphate (0·2 c.c.) and

anhydrous potassium carbonate (0·5 g.) added and the mixture refluxed on a water-bath for 14 hours. It was then filtered and the residue washed with hot acetone. On evaporating acetone from the filtrate only a very small quantity of the methylated product (XIV) could be obtained. A little more of it could be secured by treating the residue on the filter with the minimum quantity of water and filtering off quickly. After one crystallisation from rectified spirits it melted at about 190° (decomp.); Reichel *et al.*[8] recorded m.p. 191–99° for their synthetic product. It gave no colour with magnesium and hydrochloric acid in alcoholic solution, but gave a deep brown colour with alcoholic ferric chloride. But most of the methylated product was in the aqueous carbonate solution. This was directly hydrolysed by acidifying with sulphuric acid and refluxing the solution for 2 hours. After cooling it was ether extracted and ether removed by evaporation when a yellow solid separated out. When recrystallised from alcohol it was obtained as yellow flat needles and rectangular plates melting at 206–8°. The mixed melting point with a synthetic sample of 4′-O-methyl-butein (XV)[2] was undepressed. It gave an olive brown colour with alcoholic ferric chloride. Yield, 0·2 g.

(*b*) *With excess dimethyl sulphate.*—Finely powdered butrin (1 g.) was suspended in dry acetone (40 c.c.), dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (3 g.) added and the mixture refluxed on a water-bath for 30 hours. It was then filtered and the residue washed with hot acetone. On evaporating acetone from the filtrate a small quantity of the methylated product (red solid) separated. More was obtained by treating the residue on the filter with a little water and filtering and washing it with small quantities of water. The aqueous solution (A) still contained considerable quantity of it and could be directly hydrolysed. Butrin dimethyl ether crystallised from alcohol as pale yellow glistening crystals melting at 210° (decomp.). Yield, 0·2 g. It gave no colour with alcoholic ferric chloride. It was rather hygroscopic and was also contaminated with mineral matter; satisfactory analytical results could not be obtained.

Hydrolysis.—The dimethyl glycoside obtained in the previous experiment was hydrolysed by refluxing with 7% aqueous sulphuric acid (20 c.c.) for 2 hours. The solution was cooled and extracted with ether. On removing the ether a pale yellow solid separated out. It was crystallised from rectified spirits when it was obtained as colourless tiny prisms melting at 95–97°. Further quantity of this compound could be obtained by acidifying the aqueous carbonate solution (A) with sulphuric acid and heating under reflux. The compound was soluble in hot sodium carbonate solution and gave no colour with ferric chloride in alcoholic solution. The mixed

melting point with a synthetic sample of 2:4′-dimethyl butein (see below) was undepressed. (Found: C, 68·2; H, 4·9; $C_{17}H_{16}O_5$ requires C, 68·0; and H, 5·3%.)

Synthesis of 2:4′-dimethyl butein.—Isopeonol (1 g.) and isovanillin (1 g.) were dissolved in alcohol and sodium hydroxide (5 g. in 4 c.c. of water) added to the solution. The mixture was corked air tight and allowed to stand for 48 hours at the room temperature. The solution was then diluted with water and acidified with hydrochloric acid. The chalkone that separated out was extracted with ether and the ether solution washed with aqueous sodium bicarbonate to remove any isovanillic acid formed during the reaction. The ether was removed by distillation when 2:4′-dimethyl butein separated as a pale yellow solid. It crystallised from rectified spirits as colourless tiny prisms melting at 95–97°. It gave no colour with alcoholic ferric chloride and was soluble in hot sodium carbonate solution. Yield (0·5 g.). It was identical with the product of hydrolysis of dimethyl butrin described above.

Methylation of Naringenin

(*a*) *Using two mols. of dimethyl sulphate.*—The methylation of naringenin (1 g.) was carried out as in other cases using dimethyl sulphate (0·8 c.c.) and anhydrous potassium carbonate (3 g.) in acetone medium. After refluxing for ten hours, the acetone solution was filtered and evaporated. The residue obtained thereby, was sparingly soluble in aqueous alkali. It was washed twice with cold alkali and then with water. It then crystallised from alcohol in the form of colourless long rectangular prisms melting at 120–22°. Yield, 0·5 g.

An alcoholic solution of the substance developed a scarlet red colour with magnesium and hydrochloric acid and with ferric chloride, a deep reddish brown colour. It was found to be identical with sakuranetin-monomethyl ether.[9]

(*b*) *Using three mols. of dimethyl sulphate*

Naringenin (1 g.) was methylated as in previous cases using three molecular proportions of dimethyl sulphate (1·2 c.c.) and anhydrous potassium carbonate (4 g.) in dry acetone medium. After refluxing for 10 hours, the acetone solution was filtered and evaporated. A yellow semi-solid was obtained which crystallised from alcohol as lemon yellow stout prisms, melting at 112–13°. Yield of the pure product 0·5 g.

It dissolved in aqueous alkali forming an yellow solution. Alcoholic ferric chloride developed an yellowish red colour. No red colour was

noticed on reduction with magnesium and hydrochloric acid in alcoholic solution. A bright yellow colour was obtained when the substance was treated with boric and citric acids in dry acetone solution. From a mixed melting point determination, it was found to be identical with an authentic sample of 4 : 6 : 4′-trimethoxy-2-hydroxy-chalkone.[12]

(*c*) *Using four mols. of dimethyl sulphate*

The above experiment was repeated with naringenin (1 g.) and four molecular proportions of dimethyl sulphate (2 c.c.). When the acetone solution was evaporated a yellow crystalline solid was obtained. It crystallised from alcohol in the form of yellow aggregates of plates melting at 120–21°. It was insoluble in alkali and gave no colour changes with ferric chloride in alcoholic solution and also with magnesium and hydrochloric acid. It was found to be identical with a synthetic sample of 2 : 4 : 6 : 4′-tetramethoxy chalkone.[12]

Methylation of butin

(*a*) *With 3 mols. of dimethyl sulphate.*—To a solution of butin (0·5 g.) in dry acetone (40 c.c.), dimethyl sulphate (0·6 c.c.) and anhydrous potassium carbonate (2 g.) were added and the mixture refluxed on a water-bath for 12 hours. It was then filtered and the residue washed with hot acetone. On evaporating the acetone from the filtrate a yellow solid separated out. When crystallised from alcohol it was obtained as glistening yellow leaflets melting at 156°. It was identical with butein-4 : 3′ : 4′-trimethyl ether[17] and the mixed melting point with a synthetic sample was undepressed. It gave a brown colour with alcoholic ferric chloride.

(*b*) *With excess of dimethyl sulphate.*—Dimethyl sulphate (1 c.c.) and anhydrous potassium carbonate (3 g.) were added to a solution of butin (0·5 g.) in dry acetone (40 c.c.) and the mixture refluxed for 24 hours on a water-bath. It was then filtered and the residue washed with hot acetone. On evaporating the acetone solution the methylated product was obtained as a yellow solid. By crystallising from alcohol twice butein-tetramethyl ether was obtained as yellow irregular plates melting at 120–22°. It gave no colour with ferric chloride in alcoholic solution and was insoluble in alkali. The mixed melting point with a synthetic sample of tetramethyl butein described below was undepressed.

Synthesis of tetramethyl butein.—Resacetophenone dimethyl ether (0·5 g.) and veratraldehyde (1 g.) were dissolved in alcohol (30 c.c.) and potash (5 g. in 4 c.c. of water) added. More alcohol was added to get a clear solution and the mixture kept corked air tight for 48 hours at room temperature.

Then the solution was diluted and the chalkone that separated was filtered and washed with water. When crystallised from rectified spirits twice using animal charcoal it was obtained as yellow plates melting at 120–22°. It gave no colour with ferric chloride in alcoholic solution and was insoluble in aqueous alkali. It was sparingly soluble in ether but readily soluble in ethyl acetate and alcohol. (Found: C, 70·0; H, 6·3; $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%.)

5: 7-*Dihydroxy-flavanone.*—This was originally made by Shinoda and Sato[14] by condensing phloroglucinol with cinnamoyl chloride in nitrobenzene solution using aluminium chloride as condensing agent. It has now been obtained by the demethylation of 5: 7-dimethoxy flavanone with anhydrous aluminium chloride in benzene solution.

5: 7-Dimethoxy-flavanone (0·5 g.) was dissolved in dry benzene (5 c.c.), anhydrous aluminium chloride (1 g.) added and the mixture refluxed on a water-bath for 1 hour. Benzene was then removed by evaporation. The aluminium chloride complex was decomposed by treating with ice-cold dilute hydrochloric acid when the dihydroxy-flavanone separated out. This was ether extracted and ether distilled off. On crystallising twice from rectified spirits using animal charcoal it was obtained as pale grey aggregates of broad rectangular plates melting at 201–3°. Yield (0·3 g.). It gave a pink colour with alcoholic ferric chloride and dissolved in aqueous sodium hydroxide forming a yellow solution (Shinoda and Sato reported the melting point as 203°). (Found: C, 69·8; H, 4·5; $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·6%.)

5-*Hydroxy-flavanone.*—This was prepared by demethylating 5-methoxy-flavanone with anhydrous aluminium chloride.

5-Methoxy-flavanone[19] (0·5 g.) was dissolved in dry benzene (10 c.c.) and anhydrous aluminium chloride (1 g.) was added. After refluxing the mixture for one hour, the product was worked up as in the above preparation. The 5-hydroxy-flavanone crystallised from benzene (charcoal) as straw-yellow rectangular prisms melting at 152–54°. It gave a green colour with ferric chloride in alcoholic solution and dissolved in aqueous alkali on warming to form an yellow solution. (Found: C, 64·8; H, 6·0; $C_{15}H_{12}O_3$, $2H_2O$ requires C, 65·2; H, 5·8%.)

Action of alkali on some flavanones

1. *Naringenin.*—Naringenin dissolved readily in cold 10% aqueous sodium hydroxide forming a yellow solution. After half an hour it was acidified with dilute sulphuric acid when a colourless solid was precipitated.

This was filtered, washed and dried. It was identified as naringenin since it had all the required properties and reactions and the mixed melting point was not depressed.

2. *Isosakuranetin.*—It was also readily soluble in 10% cold aqueous sodium hydroxide and was recovered almost quantitatively from the yellow alkaline solution by acidification after half an hour. The melting point and colour reactions were the same as those of the original substance.

3. *Naringenin-7 : 4′-dimethyl ether.*—It was sparingly soluble in cold 10% aqueous sodium hydroxide. It however went into solution completely on warming. When acidified after keeping the alkaline solution for half-an-hour, the original compound was reprecipitated almost quantitatively.

4. 5 : 7-*Dihydroxy flavanone.*—It dissolved in cold aqueous sodium hydroxide (10%) forming a yellow solution. It could be completely recovered unchanged by acidifying the alkaline solution after half-an-hour.

5. 5-*Hydroxy-7-methoxy-flavanone.*[13]—This compound dissolved in aqueous sodium hydroxide (10%) on warming. It could be recovered unchanged by acidification of the alkaline solution after half-an-hour.

6. 5-*Hydroxy-flavanone.*—It went slowly into solution in 10% cold aqueous sodium hydroxide. The alkaline solution was yellow and deposited the original 5-hydroxy-flavanone when acidified with sulphuric acid.

7. 5 : 7 : 4′-*Trimethoxy-flavanone*[20].—This compound was synthesised by refluxing an alcoholic solution of 2-hydroxy-4 : 6 : 4′-trimethoxy chalkone[12] (m.p. 112°) containing 4% sulphuric acid for 24 hours. On evaporation of the alcohol, a mixture of the flavanone and chalkone was obtained. The components were separated by fractional crystallisation from ethyl acetate in which the flavanone was less soluble. It was finally crystallised from the same solvent when it was obtained as colourless prismatic crystals melting at 123–24°.

The trimethoxy-flavanone was insoluble in the cold aqueous sodium hydroxide (10%). But it gradually turned yellow and showed a tendency to go into solution slowly. This dissolution could be hastened by warming. The alkaline solution was yellow and when acidified with sulphuric acid a yellow semi-crystalline solid was obtained. It was taken up in ether. On the removal of ether by evaporation, a yellow oil was left behind which solidified on scratching with a glass rod. It crystallised from alcohol in the form of stout prisms melting at 112–13° and was identified to be 2-hydroxy-4 : 6 : 4′-trimethoxy-chalkone by direct comparison.

8. *5-Methoxy-flavanone*[19].—It was insoluble in cold 10% aqueous alkali, but it could be got into solution by slight warming. The alkaline solution was yellow and when acidified with sulphuric acid after half-an-hour, a yellow solid different from the 5-methoxy-flavanone, was obtained. It melted at 127° and gave a brown ferric chloride colour. It was identified to be the 2-hydroxy-6-methoxy-chalkone[19] by direct comparison.

9. *5:7-Dimethoxy-flavanone*[13].—This behaved similar to the above. When the alkaline solution was acidified after half-an-hour a pale yellow crystalline solid was obtained. It crystallised from aqueous alcohol and melted at 91–92° and in all its properties was identical with 2-hydroxy-4:6-dimethoxy-chalkone.[13]

Summary

A marked difference in the behaviour of naringin and of butrin towards hydrolysing agents has been noticed previously. Thus naringin yields the flavanone, naringenin, while butrin yields a mixture of the flavanone, butin, and the chalkone, butein. Similar difference in behaviour is also exhibited by the flavanones, naringenin and butin, when treated with mineral acids or alkalis.

Methylation has now been conducted of the glycosides, naringin and butrin and their aglucones naringenin and butin using varying molar proportions of dimethyl sulphate in the presence of anhydrous potassium carbonate and in acetone solution. From the study of the products and also of a number of simpler flavanone derivatives it is clear that the presence of a free 5-hydroxyl gives stability to the pyranone ring. This stability is not found when the 5-hydroxyl is non-existent as in butrin and butin or gets methylated as in some of the methyl ethers of naringin and naringenin and other flavanones; the products are chalkones in these cases.

The special influence of the 5-hydroxyl group in stabilising flavanone structure is attributed to the existence of chelation between this hydroxyl and the carbonyl group of the pyranone ring. The mechanism of the chalkone-flavanone conversion is discussed.

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CONDENSATION OF ALDEHYDES WITH MALONIC ACID

Part XXII. Condensation of 6-Bromo-Piperonal

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*6-Bromo-piperonal has been condensed with malonic acid in the presence and absence of pyridine, in the presence of a pyridine-piperidine mixture and in the presence of glacial acetic acid. Two products have been obtained and identified: 6-bromo-piperonylacrylic acid and 6-bromo-piperonyl-malonic acid. As in the case of piperonal-malonic acid condensation (Kurien and Pandya,[3] 1934; Pandya and Vahidy, 1936[6]), the yield of bromo-piperonyl-acrylic acid has been excellent, reaching up to the theoretical at best (in the pyridine-piperidine mixture, according to Robinson and Shinoda[10]).

Earlier workers above[3, 6] did not succeed in obtaining from piperonal, piperonylmalonic acid, thought it was obtained earlier by Knoevenagel[2] and by Piccinini[9] by other methods. The corresponding dibasic acid from 6-bromo-piperonal was not obtained, as was expected, in the condensation without any condensing agent; but it came out in the condensation in the presence of glacial acetic acid (Stuart's[11] method) in 72% yield.

The 6-bromo-piperonyl-malonic acid melted with effervescence, like all malonic acids, and was thereby changed into the 6-bromo-piperonyl-acrylic acid.

Usually the dibasic acid melts at a higher temperature than does the monobasic acid obtained from it by the removal of carbon dioxide. In the present case, however, the opposite condition prevails: 6-bromopiperonyl-malonic acid melts at 202–03°, while the 6-bromo-piperonyl-acrylic acid melts at 254°. The same is true with regard to the unbrominated piperonyl-acids; piperonyl-acrylic acid has the m.p. (according to various earlier workers[4, 8]) varying from 232° to 242°. Piperonyl-malonic acid is reported

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* The condensation in the presence of pyridine-trace was first carried out by R. B. P. in 1942 and the product was identified. R. L. S. carried out the work independently in 1946–47.

to have the melting point at 187-89° (Piccinini[9]) and 190–95° (Knoevanagel[2]), but definitely lower.

Experimental

6-Bromo-piperonal.—It was prepared according to the method of Oelker melting at 128–29° (129°, Oelker[5]). The needle-shaped cream-coloured crystals were soluble in hot alcohol, hot benzene, and in excess of ether; readily soluble in chloroform and insoluble in water. The yield was about 56%. (37% reported by Parijs[6] and 45% by Ittyerah[1]; these last did not use iodine as a catalyst, as was done now.)

Condensation in the Presence of Pyridine

1. *A Trace of Pyridine.*—6-Bromo-piperonal (1·1 g.), malonic acid (0·5 g.) and pyridine (kept under alkali and fresh-distilled (0·15 g.) were heated together for three hours (1 : 1 : 0·35 mol.). As both the aldehyde and the acid had melting-points quite above the temperature of the water-bath, it was arranged that the heating was at 105–10° for two hours and at 120° for one hour. The mass became semisolid and gave out carbon dioxide, which slackened after 15 minutes. The reacting mass became yellow and hard and remained so all the time. This was then crushed and extracted with sodium carbonate solution (warm). It was filtered, the residue was again digested with sodium carbonate solution; the residue was the unreacted aldehyde (= 0·2 g.). The total filtrate and extract, when acidified gave a white precipitate, melting, after recrystallisation at 254°, and was identified as 6-bromo-piperonyl-acrylic acid. Yield 1·0 g., 1·1 g. (on the basis of the aldehyde taken = 77%—81% of theory: on the basis of the aldehyde actually used = 94% of theory.) Its properties and analysis are given below.

2. *In the Presence of Half a Molecule of Pyridine.*—The molecular proportion was 1 : 1 : 0·5, and the heating was at 115–20° for six hours. 0·15 g. aldehyde was recovered, and the yield was 1·1 g. (*i.e.*, calculated on the aldehyde taken—81%, and on the aldehyde actually used over 98% of theory).

3. *In the Presence of Pyridine-Piperidine* (according to Robinson and Shinoda[10]).—The aldehyde (1·15 g.), malonic acid (1·30 g.), pyridine (1·20 g.) and piperidine (two drops) were treated by the above method. The mass fused within fifteen minutes, then became semi-solid, and there was a brisk effervescence: when the latter slackened, a homogeneous liquid was left, which changed to a semi-solid first and then to a light orange coloured solid. The unreacted aldehyde recovered was only 0·05 g.; and the yield of the purified product was 98·5–100%.

The 6-bromo-piperonyl-acrylic acid was crystallised from hot alcohol, and melted finally at 254°. It was almost insoluble in acetone, chloroform, carbon tetrachloride and benzene. Though when freshly crystallised it had a white colour, it always became slightly yellowish on keeping even in a corked tube. It immediately decolourised Baeyer's reagent as well as bromine water in the cold. [Equivalent weight found = 270·1, 271·9 by titration (in hot alcohol against standard sodium hydroxide solution). $C_{10}H_7O_4Br$ requires equivalent weight = 271·0. Found: Br, 29·54, 29·23%. $C_{10}H_7O_4Br$ requires Br, 29·52%.]

In the Absence of Any Condensing Agent

The aldehyde and malonic acid were heated alone (in 1 : 1 mol.) on water-bath; even after 2 hours, no fusion and no condensation took place. The same thing happened when the heating was carried out at 105–10°. The aldehyde sublimed away.

In the Presence of Glacial Acetic Acid (according to Stuart[11])

(1) The same amounts of the aldehyde and malonic acid were heated on water-bath with 2 c.c. of glacial acetic acid (1 : 1 : 3·5 mol.) for 11 hours. Within 10 minutes, a clear liquid was formed, and a yellowish red colour appeared. 0·2 g. of unreacted aldehyde was recovered, and a product recovered in the usual way: it was a yellowish solid, which on shaking with ether and on evaporation of the ether later, gave fine yellow crystals (needles): the melting-point, after purification, was 202–03°. This was the 6-bromo-piperonyl-malonic acid. It weighed 0·9 g. (*i.e.*, 59·6% on the aldehyde taken or 72·6% on the aldehyde used).

(2) In another experiment more of glacial acetic acid was taken (1 : 1 : 5 mol.). The heating was for 13 hours at 100–105°. The yield however was lower (50·6%).

(3) The quantities were as in (1), the temperature was 100–05° and the heating was for only 6½ hours. The yield was still less (29·7%).

When absolute alcohol was taken, instead of the acetic acid, in sufficient quantity (7 c.c.), and the reactants were refluxed on water-bath for 14½ hours, resinification was found to have taken place and nothing could be separated.

The 6-bromo-piperonyl-malonic acid had a bright yellow colour: various methods of purification left the melting-point unchanged (202–03°, with effervescence and decomposition). It was soluble in alcohol, but less so in chloroform and benzene (warm). After melting at 202–03°, and after

the effervescence had stopped, a solid was left behind, which melted only at 250° (without effervescence), showing that the dibasic acid had changed into the mono-basic 6-bromo-piperonyl-acrylic acid (m.p. 254°). This was confirmed by means of the identical mixed melting-point with a specimen of the monobasic acid. Equivalent weight found (by titration of alcoholic solution) 158·3; $C_{11}H_7O_6Br$ requires equivalent weight = 157·5. Found: Br, 24·93. $C_{11}H_7O_6Br$ requires Br, 25·39%.

Summary

6-Bromo-piperonal has been condensed with malonic acid and gives two different products; 6-bromo-piperonyl-acrylic acid (the highest yield being quantitative) and 6-bromo-piperonyl-malonic acid (the highest yield being 72%). The presence of pyridine gives the first, that of glacial acetic acid gives the second.

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ERRATA

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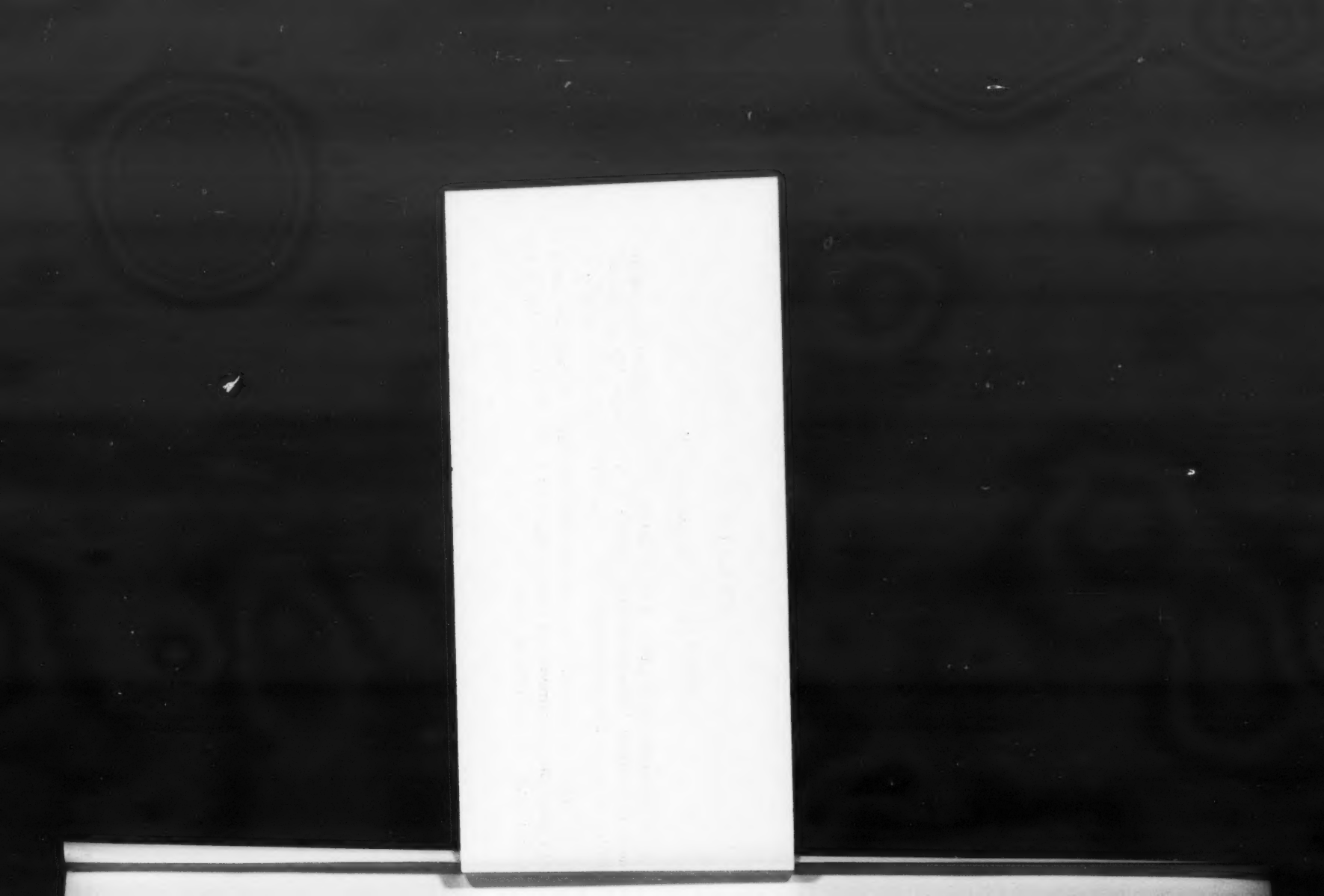
1. Transfer the heading "Determination of minimum time required to cause fatal injury " appearing after " Table II " on page 124 to appear before the paragraph commencing with " The solid drugs " on page 125.

2. *Insert* a new line " Calycopterin dimethyl ether " *between the lines* " Calycopterin–4′–monomethyl ether + Bile salts " *and* " Calycopterin and Gum acacia " in Table II on page 124.



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